Clinical Medicine

volume 7/number 1

January
1960

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JANUARY, 1960 *Volume 7, Number 1*

editorial

original articles

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Clinical Medicine

JAMES M. NORTHINGTON, M.D., *Editor-in-Chief*

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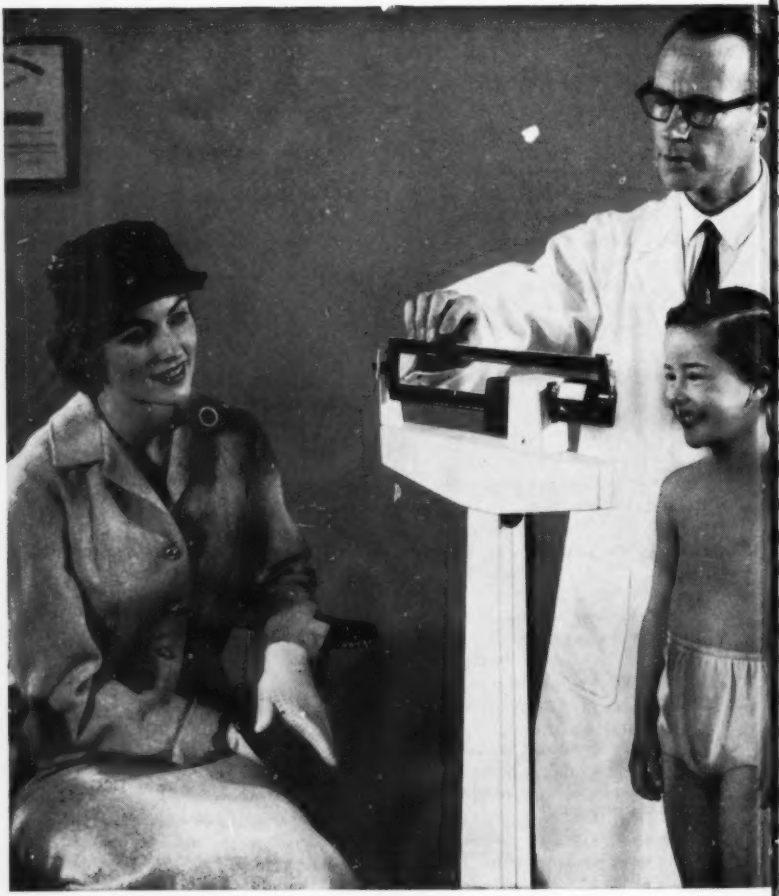
Underweight Children Gain an



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---

*Brown, S. S.; Libo, H. W., and Nussbaum, A. H.: Norethandrolone in the Successful Management of Anorexia and "Weight Lag" in Children, Scientific Exhibit presented at the Annual Meeting of the American Academy of Pediatrics, Chicago, Oct. 20-23, 1958.

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(1) Wallerstein, R. O., and Hoag, M. S.: J.A.M.A. **164**:962 (June 29) 1957. (2) Eastman, N. J.: Current M. Dig. **25**:55 (Jan.) 1958. (3) Koszewski, B. J., and Walsh, J. R.: Am. J. M. Sc. **235**:523 (May) 1958. (4) McCurdy, P. R.; Rath, C. E., and Meerkrebs, G. E.: New England J. Med. **257**:1147 (Dec. 12) 1957.

LAKESIDE

Teaching in a Rural Hospital

HAROLD B. PLUMMER, M.D., *Preston, Maryland*

►*Few realize the increasing importance of the rural general practitioner and the excellent opportunity he has to raise the standards of the nursing profession in the rural hospital, to maintain good relations between the hospital and the community, and to assist in the postgraduate training of physicians.*◄

Teaching in a rural hospital can be divided into three categories: teaching nurses, teaching resident physicians, and postgraduate instruction for the staff. In our hospital's nurses' training school, it is the duty of all the active staff members to do some teaching. The rural general practitioner, when he comes into the community, should volunteer his services for teaching nurses. This shows his interest in staff privileges, helps to increase his stature with his new associates, and is an ethical form of advertising. Some of us will do well; others who do not should be gradually weeded out.

If the doctor is well qualified, there are many mutual advantages. The doctor takes pride in his work, and is trying constantly to improve it. It enables him to keep abreast of the newer advances, and thus become better able to serve his community. It gives him more than a passing interest in his hospital, and encourages him to improve the status of his workshop. The rural general practitioner needs to press his efforts in his hospital as hospital competition is very great; and until he has manifested his interest, the "old guard" is going to consider him only according to his past record. The plight of the physician in reference to present hospital relations is, in many instances, of his own making. It may be possible for the general practitioner to re-establish the real purpose of the hospital; i.e., to serve the patients, not, as it is considered by many specialists, to serve the specialists.

The doctor's interest and desire to do good work improves the service and the standing of the hospital. It promotes better relations between the staff and the

governing board of the hospital, enabling them to better serve the community.

Hospital Administration

Of course, the administrator, board of governors and staff have separate and distinct purposes; yet, if the hospital is to run efficiently, the efforts of all must be coordinated. Neither is *in*dependent; all are *inter*dependent.

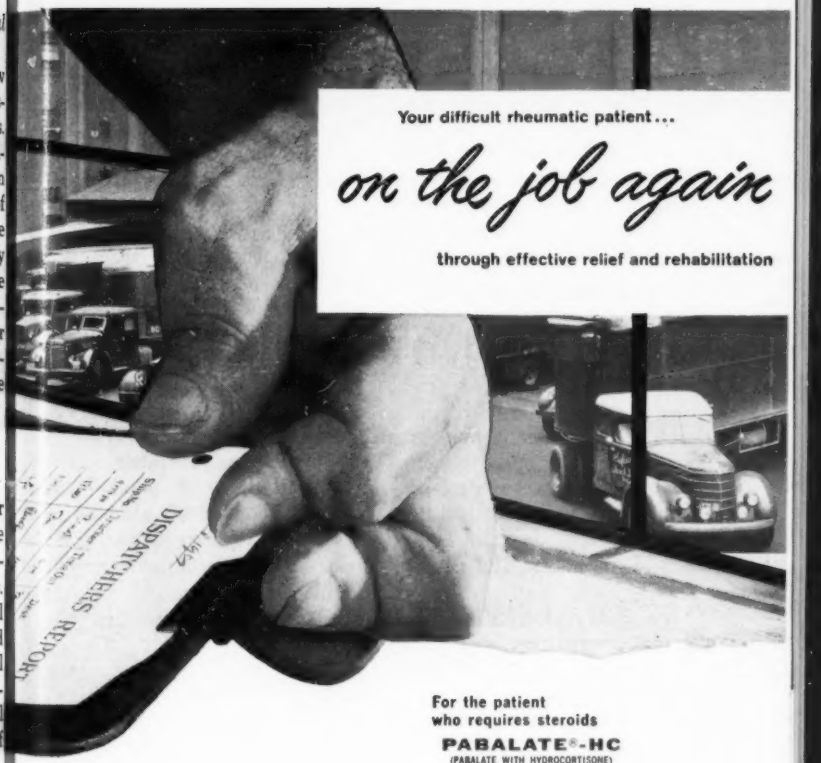
There is a recent recommendation from the American College of Surgeons that every hospital should have one or more members of its active medical staff serve as elected members of the board. Joint conference committees can not solve all problems as well as can intimate, personal contact. This consideration is especially important in light of the ever-increasing number of hospitals which are being run exclusively by the administrator or a combination of the administrator and the board. Doctors on the board will help to bring the hospital back to the patients. The rural general practitioner is the greatest factor in the improvement of relations between all of these units; because he has the most contacts with the general public—his patients.

The cooperation of doctors is the one way doctors can help to improve the nursing profession's standing in the community as a whole, because then we know what is being done for the nursing profession as undergraduates. This leads to a better understanding of each other's problems. In an effort to raise the stature of the degree R.N., many fields are being explored. There are many efforts being made to associate schools of nursing with institutions of higher learning, in order that the graduate nurse may receive a degree comparable to the A.B. or B.S. degree.

Role of the Rural General Practitioner

The rural general practitioner fits well into this picture. We have neglected many opportunities to improve our relations. With an upsurge in the general practitioner's standing, we should make full use of this wonderful opportunity. Except in the highly specialized fields, the general practitioner is the best teacher of nurses. He must bring his knowledge to the level of an undergraduate student, as he is constantly doing with his patients. He is well qualified to teach medical nursing, anatomy, physiology, pharmaceuticals and all other subjects of this nature.

All of us should encourage, through our rural hospitals, the formation of general pratice residencies in our nearby medical schools. This is a corollary to the above procedures; the rural hos-



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pital should, by all means, be a part of this program. The forementioned points lead to the last, that the department of general practice in every rural hospital should gear itself to the training of more and more general rural practitioners.

General Residency Programs

Intern and resident programs in the rural hospital are quite a problem because of the great number of openings in both fields; and unless the medical school uses a good accredited rural hospital for their general residency program, not only will the rural hospital suffer, but also the future doctors of medicine. The reasons for this are many: the wards of large hospitals no longer exist, the outpatient departments are no longer crowded, and both these facts lessen the amount of clinical teaching. The rural or semi-rural hospital is rendering an increasing amount of medical and surgical care, as patients desire to be close to home and more such hospitals are being constructed. The urban district of large cities is shrinking; the suburban and rural areas are becoming more populated. The training of doctors, particularly general practitioners will soon have to include the rural and semi-rural hospital in order for internes to get a rounded background for general practice.

Better Staff Conferences

The postgraduate training for the physician of the staff should consist of good staff meetings with business kept at a minimum, sectional and departmental organization with adequate and expert discussion of cases within each section, good rounds conducted by competent members of the staff, the use of good medical films, the use of closed-circuit television, where feasible, and the use of members of nearby medical faculties at various times during the year. Staff meetings are a bore to many doctors. They are compulsory to maintain active staff privileges, and often they are a complete waste of a good evening that could be better spent with the family or a good book. Administrative matters should be reduced to a minimum. Seminars should be encouraged in order to better train each staff physician. These could easily be conducted by efficient heads of the various departments.◀

The Nodular Thyroid and Thyroid Cancer

ROBERT S. POLLACK, M.D., *San Francisco, California*

► *About 70 per cent of thyroid carcinomas are papillary, the remainder being either pure alveolar and follicular forms, or of the highly malignant types. Although few are said to die from thyroid cancer, follow-up studies of periods of ten years have shown a cure rate of only 20 to 30 per cent.*◄

The physician confronted with a thyroid problem must differentiate between two broad groups of thyroid diseases: physiologic toxicity, and neoplastic disease—totally different conditions, requiring different management. This paper deals with neoplastic thyroid disease.

Incidence

The incidence of cancer in thyroid nodules varies greatly—from 4% in North Carolina and 4.8% in California to 24.5% in Cleveland, Ohio. At Stanford University Hospital and the University of California Hospital in San Francisco, far less thyroid disease is seen than in the Middle West. In the California hospitals about 5 per cent of all nodules removed are malignant. At the University of California Hospital a recent pathologic study of thyroid disease stimulated much interest in thyroid cancer. All of a sudden the incidence of thyroid cancer in the operating room increased to 18 per cent. In the Midwest, similar incidences have been reported, but along the Eastern seaboard, the incidence is closer to 4 to 8 per cent.[1-3]

These figures emphasize the importance of defining exactly what is meant by "a nodule." If a gland has multiple nodules, without spaces or delineations between, it is most likely that we are dealing with involutional change only. When a gland contains several independent nodules in one or both lobes, the probability of neoplastic disease is far greater.

Today, each nodule is evaluated first on the basis of a thorough history and physical exam-

1. Cole, W. H., et al., *J.A.M.A.*, 127:853,1945.
2. Crile, G., Jr., & Dempsey, W. S., *J.A.M.A.*, 139:1247,1949.
3. Hinton, J. W., & Lord, J. W., Jr., *J.A.M.A.*, 129:605,1945.

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*Swartz, H.: To be published.

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ination. Is the nodule a neoplasm, or is it merely one phase of the involution of the thyroid gland? Next, patients with thyroid nodules are given radioactive iodine for uptake studies.[4] A discrete nodule, 2 or 3 cm. in diameter, whose uptake of radioiodine is large, is probably not a true neoplasm, although some adenomas will take up radioiodine, and a course of treatment with thyroid extract outlined. These are referred to as "hot" nodules, probably involutional. If after three months of thyroid medication the nodule persists, one would consider surgical removal. For the "cold" nodule, no uptake of radioiodine—prompt surgical removal is best treatment. Even here the vast majority of cold nodules are not malignant, but they are neoplastic.

The thyroid gland with multiple small nodules presents a problem on scintogram. Radioiodine studies in these instances are difficult to obtain with accuracy because each nodule tends to obscure the scanning technique. Therefore, when accurate scanning cannot be performed, surgical removal is deemed wisest. The very small nodule is also difficult to scan accurately, and in all probability it, too, should be removed.

A reported incidence of 20 per cent, or 8 per cent, malignant disease in thyroid nodules should be qualified. These figures represent operating room experience, it has been noted that the surgical material studied represented a screened and selected incidence.[2] There are many more patients in good health with thyroids containing solitary or multiple nodules who never come to surgery. Though the true incidence of thyroid cancer in nodules is very small, this should not lead one into a false sense of security. It is far more prudent to assume that each patient with a thyroid nodule might have thyroid cancer, and that he must be individually studied.

About Nodular Goiter Becoming Cancerous

The percentage of cases in which nodular goiter becomes cancerous has also been the subject of numerous autopsy studies.[1,5] However, autopsy material does not provide a true index. In the period 1944 to 1948, there were 675 autopsies at the Illinois Research Hospital.[1] In only two cases was thyroid cancer found. During this same period, 16 patients with thyroid cancer were operated upon. Of this number, 11 were known to be dead but autopsy was not done on any of them at the Illinois Research Hospital.

4. Groesbeck, H. P., *Cancer*, 12:1-9,1959.

5. Dailey, M. E., et al., *Am. J. Med.*, 9:194-200,1950.

Clinical Observations

In a review of patients with thyroid cancer[6-8] certain clinical findings were noted. Age is not an important factor, the range being six to 86 years. Thyroid cancer in children has become far more prevalent during the past five years, often associated with a history of irradiation to the lower portion of the neck. This is so in a considerable number of cases of thyroid cancer seen in children, and merits emphasis.[9] In many instances the child had been subjected to irradiation, presumably for thymic enlargement. Then, some 10 or 12 years later, we find cancer of the thyroid in the child. A nodule in the thyroid gland of a child should be taken with especial seriousness and the possibility of cancer entertained.

Carcinoma arising in diffuse toxic goiter is rare, and toxicity occurs infrequently in patients with thyroid cancer. When toxicity is manifested, the carcinomatous area is not usually responsible for the hyperthyroidism.[10] In a personal series[6-8] there was a rather high incidence of toxicity in those patients who had thyroid cancer, seven out of 63 patients, perhaps an exception to the rule.

6. Pollack, R. S., *California Med.*, 74:365-370,1951.
7. Pollack, R. S., *Arizona Med.*, 15:803-807, 1958.
8. Pollack, R. S., *Tumor Surgery of the Head & Neck*, Lea & Febiger, Philadelphia, 1957, p. 71.
9. Clark, D. E., *J.A.M.A.*, 159:1007-1009,1955.
10. Friedel, M. T., *Arch. Surg.*, 43:386,1941.

The incidence of thyroid cancer is higher in females, but because the solitary nodule in a male is less frequently seen, its chance of being malignant is proportionately higher. Twenty-five per cent of the patients in this series had recurrent tumors, and were seen following treatment to the thyroid at some previous time. Of the 63 cancers, 16 occurred in patients with a nodule as the presenting sign. Of these 16, 12 were solitary nodules and four were multiple. This fits in with a growing feeling that multiplicity of nodules in the gland is not a sure sign against the presence of cancer, although it is true that the solitary nodule, especially in the male, is the more dangerous clinically.

Diagnosis

It was possible to make a clinical diagnosis in half of the patients in this series, due probably, to so many having cervical node and distant metastases with a thyroid tumor. In over half, the tumor was present for less than 24 months. This is noteworthy because it has been said that thyroid cancer is a slow growing disease, that one has time to act on it, and that one can observe it clinically for long periods before doing anything specific. It has been stated also that this form of cancer does not metastasize quickly. The figures do not support these con-

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tentions. Half of the patients had lesions for less than one year. These were clinically evident and showed increased size, and all patients gave a high incidence of cervical node and more disseminated metastases.

A fixed or hard tumor causing symptoms of pressure on the trachea or esophagus is usually cancer. The signs and symptoms most frequently noted are: fixation, especially to the underlying trachea; hardness, often described as "stony"; hoarseness, without soreness or pain; slow, asymptomatic enlargement of lateral lymph nodes; and later dyspnea and dysphagia. A history of a long-standing solitary nodule which suddenly increases in size is significant. One patient reported that six months before she sought medical advice she noticed enlargement of a nodule which had been present for 10 years. Six months after the first examination the patient died of widely disseminated metastases from a giant-cell carcinoma of the thyroid.

Metastases

Although thyroid cancers frequently invade the blood stream, the most common avenue of spread is through the lymphatic system. Lymph-borne metastases occur first in the cervical and later in the mediastinal nodes. The cervical lymph nodes of predilection are those in the posterior triangle of the neck along the transverse cervical chain*, or those of the middle and superior groups along the internal jugular vein. More rarely, metastases occur in nodes in the submaxillary triangle. In several cases metastasis to an axillary node has been observed. Three patients in the study had such metastases in addition to spread to other sites.

There were 30 patients who had metastases when first observed. 20 of these to the cervical nodes only. Of 18 patients with accurately described nodal metastasis, 10 had involvement of the transverse cervical group of nodes, seven of the middle and superior jugular groups, and one of the submaxillary triangle group.

In several cases in which cancer in laterally placed cervical lymph nodes was observed, a diagnosis of cancer arising in lateral aberrant thyroid tissue was erroneously made. After years of study it is now realized that the growths in those nodes are metastatic from a small, primary cancer tucked away in the thyroid gland, usually not palpable and not known to be present until the lobe is rotated out of its bed.

Classification

There are parallels between the morphologic pattern of thyroid tumors and their clinical mani-

*This group of lymph nodes follows the transverse cervical artery.

Table 1.

Classification of Thyroid Cancer

I. **Low-Grade or Potential Cancer:**
   1. Adenoma with blood vessel invasion.
   2. Papillary cystadenoma with blood vessel invasion.

II. **Moderately Malignant:**
   1. Papillary adenocarcinoma.
   2. Alveolar adenocarcinoma.
   3. Hurthle-cell adenocarcinoma.
   4. Solid adenocarcinoma.

III. **Highly Malignant:**
   1. Small-cell carcinoma (carcinoma simplex).
   2. Giant-cell carcinoma.
   3. Epidermal carcinoma.
   4. Fibrosarcoma.
   5. Malignant lymphoma.

festations. The clinical picture varies with the type of tumor. A classification[5,11-13] (Table 1) enables the clinician to gauge the clinical course once the histologic nature of the lesion is known.

The so-called malignant adenomas, or poorly defined "almost" cancers, are listed in the potentially malignant group. Some of these adenomas show blood vessel invasion despite a benign histologic appearance. Others show papillary projections and formations but appear benign histologically. These too, are indeed, malignant[14] despite their low-grade histologically.

In some cases the clinical course of papillary tumors is extremely long, and as a consequence doubt is cast on the diagnosis of cancer. Papillary tumors occur most frequently in young adults. Thyroid cancers of youth and childhood are preponderantly papillary.

Certain cancers of the alveolar type are misdiagnosed and not called cancer on pathologic examination of the operative specimen, owing to their extremely orderly structure. Months or years later a distant metastatic deposit may occur in the skeleton or elsewhere giving rise to the term "benign metastasizing struma".

Giant-cell tumors of the thyroid gland are extremely malignant. Frequently death is caused by obstruction of the trachea or esophagus, and, although visceral metastases occur, there is rarely time for them to develop. Patients in the first two groups (Table 1.) can be treated surgically with a fair success. In the third group,

11. Warren, S., *Am. J. Roentgenol.*, 46:477, 1941.
12. Means, J. H., *Thyroid and Its Diseases*, Second Edition, J. B. Lippincott Co., 1948, p. 453.
13. Frazell, E. L., & Foote, F. W., *J. Clin Endocrinol.*, 9:1023,1949.
14. Searls, H. H., et al., *California Med.*, 76: 62-66,1952.

surgery appears to be an almost hopeless gesture because of the tremendously high incidence of early and widespread dissemination.

Method of Treatment

The trend in the treatment of thyroid cancer is toward the more radical,[1,6,8,13,15,16] the ultimate being hemithyroidectomy (or total thyroidectomy) in continuity with radical neck dissection. Total lobectomy with frozen section is recommended for solitary tumors. Not only will this remove a malignant tumor more adequately, but it is felt that the presence of one adenoma often results in the formation of another within the same lobe, and the problem of recurrence has then to be dealt with. For the tumor in the isthmus, a wide resection, including one lobe or portions of both lateral lobes, is advisable. Multiple adenomas are treated by total or near-total thyroidectomy.

Neck dissection is reserved for patients in whom the primary tumor has invaded the capsule, has involved the surrounding musculature, or has metastasized to cervical nodes. It includes removal of the internal jugular vein and sternocleidomastoid muscle and also (in view of metastasis to this area observed recently in several cases of thyroid cancer) dissection of the submaxillary triangle. The musculature overlying the involved lobe is removed in continuity with the contents excised in the neck dissection and lobectomy. In cases in which the growth is extensive it may be unwise to preserve the recurrent laryngeal nerve—better to sacrifice this structure in the interest of cleaner dissection.

There is no general agreement upon this method of treatment. Some[2,17,18] are not convinced that radical resection will improve materially the ultimate result. The problem of early invasion of veins is also to be considered, but the invasion of thyroid tumors into a vein may remain localized for a long time, a true embolus not forming for months or even years. The long survival of patients who have thyroid cancer with vein invasion is pertinent. The tendency of recurrent thyroid cancer to invade veins and the need for wide and radical removal of the veins with the tumor has been well stressed.[19,20]

If the tumor has grown into the thyroid cartilage on one side, removal of the cartilage is preferable to cutting across invaded tissue. Thyroid cancer grows backward onto the trachea and esophagus, but frequently these

15. Frazell, E. L., & Foote, F. W., *Cancer*, 11: 895-923,1958.
16. Personal communciations.
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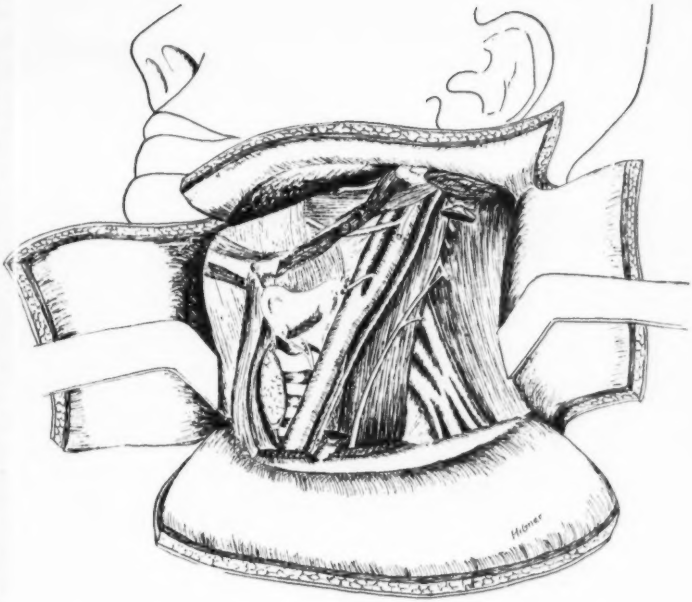


FIGURE 1
Thyroid lobectomy and ipsilateral radical neck dissection.

structures will be attached to the cancer, without being involved by it. In a neck operation requiring much dissection across the tracheal bed, tracheostomy at the close of the procedure is advisable.

A frequently seen example of thyroid cancer: A young woman with the chief finding of a solitary lump in the lateral portion of the neck, probably present for six or more months and showing slow but progressive growth. No other lumps are felt in the neck and the thyroid is normal. On the removal of the lump, it will be found to be composed entirely of thyroid tissue. There is little doubt that such a lesion in this region of the neck is a lymph node metastasis from a small cancer in the homolateral lobe of the thyroid, and not, as has been thought, an "aberrant thyroid" cancer.

Because the primary tumor is in one lobe of the thyroid, and has metastasized to the ipsilateral cervical lymph nodes, many

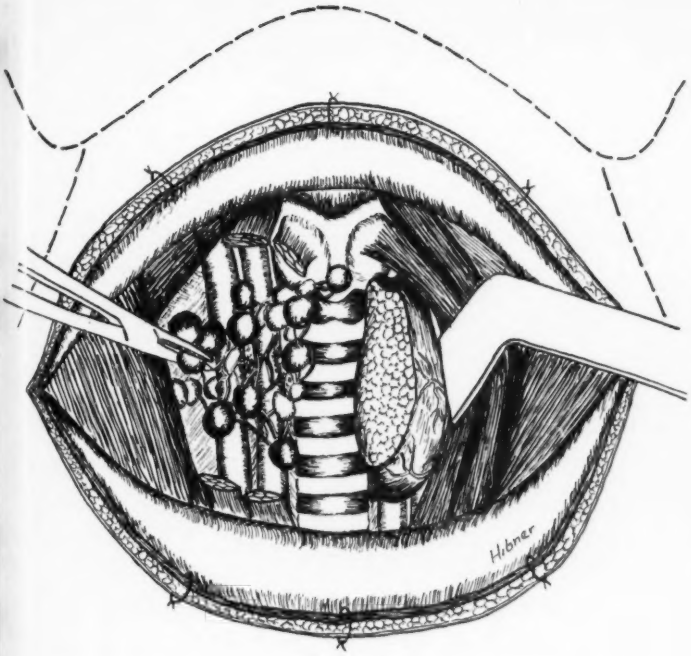
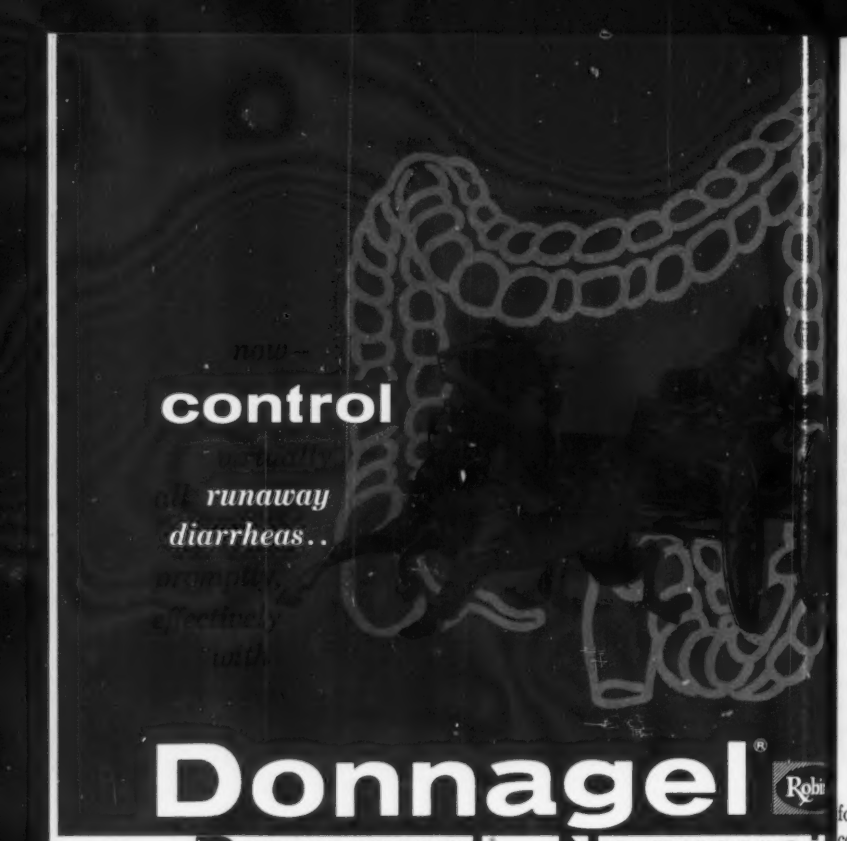


FIGURE 2
Thyroid lobectomy and removal of enlarged lymph nodes.

urgeons would recommend a hyroid lobectomy and ipsilateral eck dissection. (Fig. 1). Others, owever, equally astute, would avor a procedure removing only he involved lobe of the thyroid nd the enlarged lymph node (Fig. 2). Still others of equal authority would perform a total thyroidectomy and some of the ymph nodes of the neck on both ides. And there are some who ould remove the thyroid lobe and the lateral neck nodule and then treat that side of the neck with irradiation.

It would seem logical, however, that when a patient has a metastasis in the cervical lymph nodes of the neck, and the homolateral thyroid lobe is found to be the primary site, the cancer is spreading in a lateral direction and to remove all cancer-bearing tissue a radical neck dissection and hemithyroidectomy should be per-



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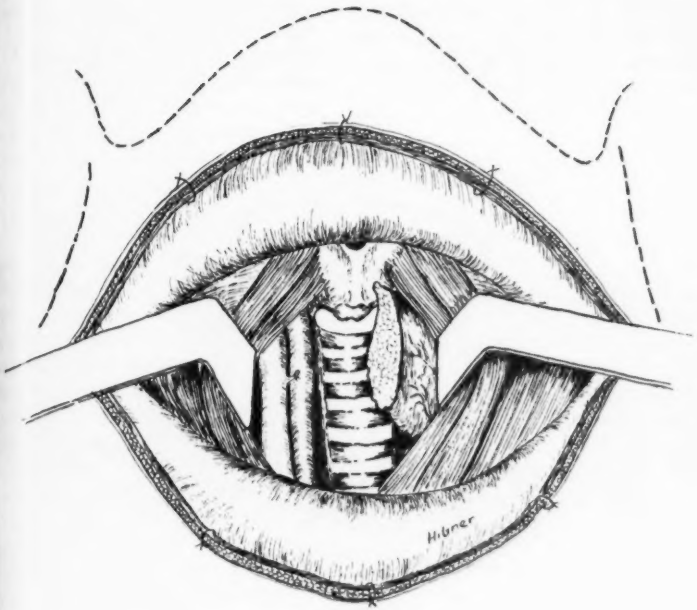

FIGURE 3
Extracapsular thyroid lobestomy.

formed (Fig. 1). This is the most common method of treating unilateral thyroid cancer which has involved the ipsilateral cervical lymph nodes.

Consider the embryological development of the thyroid. Except for the pyramidal lobe, most of the thyroid gland develops as a bilateral organ from buds at the sides of the neck where the branchial clefts and pouches are located and fuses anteriorly at the midline. The small implants of normal thyroid tissue found in the lateral muscles of the neck, especially the sternocleido mastoid, give evidence of this embryonic migration.[21] Because this thyroid tissue migrates with its own blood and lymphatic supply, one can assume that when cancer on one side of the thyroid spreads, it will spread most frequently to the same side of the neck. The incidence of crossed metastasis within the thyroid gland is debatable, as is the theory that the thyroid gland is a large venous and

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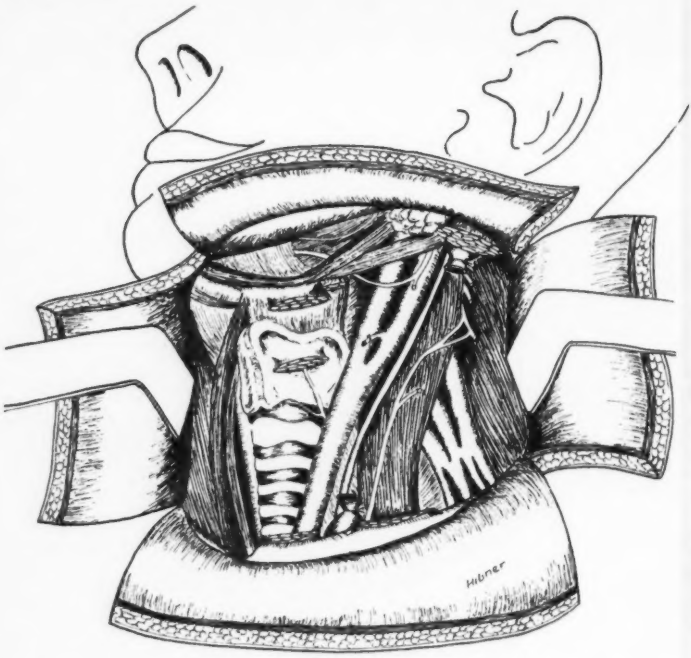

FIGURE 4
Total thyroidectomy and unilateral radical neck dissection. This procedure is recommended because of crossed metasoastis within the thyroid gland. Neck dissection is performed on the side with involved lymph nodes.

lymphatic lake in which cancer cells are trapped and disseminated intraglandularly.[22]

The incidence of a cancer in one lobe metastasizing to the other lobe appears to be under 5 per cent, although figures up to 20 per cent are reported.[22] It is still recommended, in treating a unilateral thyroid cancer,[6,15] that the involved lobe up to the midline of the neck be removed, and no more. If there are lymph node metastases on that side of the neck, or invasion of the overlying capsule and musculature, a neck dissection on that side is advised, preferably a radical one. If, however, there is only a solitary, unilateral lobe cancer, the treatment of choice is unilateral total lobectomy (Fig. 3).

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Radium and X-rays in Some Cases

Although the treatment of thyroid cancer is primarily a surgical problem, radium and x-ray treatment can be effective against tumors of certain types, particularly papillary tumors. When the surgeon feels confident that no cancer remains following operation there appears no reason for irradiation of the site as a prophylactic measure. Accurate roentgen therapy to residual disease has proved of help, when given in large enough amounts. As such therapy is not without sequelae, it should not be undertaken lightly. Surgical and x-ray treatment may be combined in otherwise hopeless cases for possible palliation. Occasionally, patients who are treated with x-ray alone because deemed inoperable, will live for three or more years.[6]

Radioactive Iodine in Toxic Thyroid Disease

Radioactive iodine has given encouraging results in the treatment of *toxic* thyroid disease if the uptake of I^{131} by the thyroid gland is large. Unfortunately, in only a few cases will the cancer pick up radioactive iodine, and in those few the amount is often too small to be of therapeutic value. Apparently the faculty of up-take possessed by a normal or toxic thyroid gland is lost when carcinoma develops. Except in an occasional case, radioactive iodine has contributed little to the specific therapy of thyroid cancer. It is, nonetheless, worthy of trial, especially in cases of skeletal metastases.

Results of Therapy

It has been said that few people die of thyroid cancer, that this is a relatively benign disease, and that the method of treatment seems not to play a great part in the cure rate. On this point the survival rate of patients in this series was carefully examined.

About 70 per cent of patients with thyroid cancer have a mixed, papillary type of adenocarcinoma. The remaining patients have malignant adenomas — a few have pure alveolar and follicular forms, and the rest highly malignant types. Of patients with papillary tumors followed, over half were alive and well without evidence of disease at the fifth year, the highest survival rate of all the histologic types, exclusive of the malignant adenomas. In other words, this group of patients still maintained the highest number of five-year cures, and this group constitutes the majority of thyroid cancers. But at 10 years the papillary carcinomas show a survival figure no better than the unclassified, or mixed type of cancers or the more malignant ones.

This fact is emphasized by the

figures on 60 patients followed for 10 years, a cure rate of only 20 to 30 per cent (determinate and indeterminate)—no dramatic or encouraging result from treatment of thyroid cancer. Since patients do not die from thyroid cancer until it spreads and extends, and since in the majority early spread is to regional lymph nodes, perhaps more aggressive primary therapy will increase survival rates. In addition, one may well reconsider the initial statement made regarding removal of thyroid nodules. Would it not be best, when in doubt, to remove all nodules of the thyroid gland. If the nodule is malignant and one projects that patient 10 years ahead, he will have, according to these figures, only three changes in 10 of surviving. The situation again may be referred to the surgeon who said that we would never have to worry about thyroid cancer if all thyroid nodules were removed.◀

Heterogenous Bone Implants

The histological, clinical, and roentgenographic response in 2 types of heterogenous bone implants in tooth sockets of 15 patients was compared. In each patient at least 4 teeth were extracted, half the sockets being allowed to fill with blood clots as controls. The remaining sockets were slightly underfilled with either "despeciated calf bone paste" (prepared by mixing 10% fibrinogen with cancellous bovine bone pretreated for at least 30 days with 20% bovine plasma) or anorganic bone chips (prepared by treating bovine bone with the organic solvent, ethylenediamine). Biopsy specimens and roentgenograms were taken 7, 14, 35, 50, 120, and 180 days after implantation. There were no obvious sensitization reactions. It is concluded that:

1. The microscopic changes occurring in the healing socket are not necessarily revealed by roentgenographic or clinical examination.

2. Although microscopic studies showed formation of fibrous tissue and eventual new bone with each type of implant, osteogenesis is not stimulated.

3. Healing frequently takes place in spite of (not necessarily because of) what is implanted.

4. More long-term roentgenographic and histologic studies in human beings are needed before the use of heterogenous bone can be properly evaluated.

Bell, W. H., *J. Oral Surg., Anesth. & Hosp. D. Serv.*, 17:3-13,1959.

Evaluation of Trimethobenzamide as an Antiemetic in Nausea and Vomiting Associated With Neoplasms

OWEN W. DOYLE, M.D., *Greensboro, North Carolina*

►*Two of the more common symptoms associated with many diseases and those most frequently mentioned as a side effect are nausea and vomiting. In a study of 63 patients in the terminal stages of cancer, 57 were completely or partially relieved within one hour following administration of this antiemetic.*◄

Possibly the most distressing symptoms accompanying neoplasms, aside from pain, are nausea and vomiting, since they weaken the already debilitated patient by interfering with proper nutrition. Any one or a combination of the following factors, by stimulating the chemoreceptor trigger zone (CTZ) and thus also the vomiting center in the medula oblongata,[1] may bring on nausea and vomiting:

1. Involvement of the gastrointestinal tract.
2. Spread of the tumor to the liver, to the abdominal lymph nodes or adjacent structures or through the central nervous system.
3. Analgesics such as narcotics, hypnotics, nitrogen mustard, etc.
4. Radiation therapy.

Associate Professor of Radiology, Duke University School of Medicine, Durham, N. C.

1. Borison, H. L., & Wang, S. C., *Pharmacol. Rev.*, 5:193,1953.

Incidence of Nausea and Vomiting From Radiation Therapy

Clinicians often expect patients receiving radiation therapy to be nauseated. Actually nausea and vomiting from radiation therapy alone occur in less than 20 per cent of the cases. The medical management of a patient with neoplasm usually includes the use of hypnotics and narcotics along with such drugs as nitrogen mustard, TEM, and chlorambucil, and when radiation is added, it is virtually impossible to isolate any one item in the treatment as the cause of subsequent nausea.

Mode of Action of Remedies Not Clear

Certain of the antihistamines and phenothiazines have been the most widely used agents for the treatment of these symptoms. It is not clearly understood just how the antihistamines work to prevent emesis, but it is known that they exert a central anticholinergic or parasympatholytic action. Their chief drawback is the production of drowsiness in a large proportion of patients.[2] Chlorpromazine, a phenothiazine derivative, which among other therapeutic effects inhibits vomiting, until recently was the only drug known to act by selectively suppressing the reflex action of the CTZ.[3] However, chlorpromazine produces many side effects, some of which may be serious.[4,5]

A Chemically Unique Agent

Trimethobenzamide*, a substituted benzamide unrelated to the antihistamines or phenothiazines, also apparently acts directly on the CTZ, but unlike chlorpromazine has no other pharmacologic effect. In a series of animal experiments in which trimethobenzamide and chlorpromazine were compared it was concluded that both appeared to act specifically on the CTZ but chlorpromazine, in addition, caused sedation, depression of behavior and a prolonged drop in blood pressure.[6] In tolerance studies patients received a total dose of 87 gm. trimethobenzamide over a period of 30 weeks without ill effects,[7] while other investigators found no laboratory abnormalities in their patients during medication with this agent.[8]

Trimethobenzamide was used with excellent effect in controlling nausea and vomiting in cancer patients undergoing radiation therapy.[9-11] Because of this success and since the aim of treatment is to make the patient as comfortable as possible without compromising the underlying therapy and without the complication of side effects, it was decided to evaluate this agent by these

*Tigan™, Hoffmann-La-Roche, Inc., Nutley, New Jersey.

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4. Nelson, N. M., *New England J. Med.*, 260:1296,1959.
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8. Roseff, I., et al., *J. Newark Beth Israel Hospital*, 9:189,1958.
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1. Lehrer, H. W., et al.: Northwest Med. 75:1249, 1955.
2. Smith, Richard T.: New York Med. 8:16, 1952

criteria in patients with neoplasms who required an antiemetic drug.

Materials and Methods

Sixty-three patients with neoplasms, and in the terminal stages of the disease, who were under radiation therapy at the start of this study or had completed x-ray treatment were given trimethobenzamide for the relief of nausea and vomiting. The symptoms were caused by radiation therapy alone in 21 cases (Group 1), narcotics plus radiation therapy in 11 (Group 2), a combination of drugs (narcotics, nitrogen mustard and chlorambucil) in 12 (Group 3), and by the extent and vital location of the disease in 19 (Group 4).

The average dosage was 600 mg. orally in all patients except those in Group 4, who received 800 mg. by the same route.

A numerical evaluation scale was employed, 0, 1, 2, and 3, indicating that pre- and post-medication nausea and/or vomiting were absent, mild, marked or severe.

Results

The average length of time between administration of the drug and onset of relief was 30 minutes for Group 1, 35 minutes for Group 2, 45 minutes for Group 3, and one hour for Group 4. This shows delayed onset with more complex therapy and increased severity and spread of the disease. When relief was obtained, it lasted 3 to 4 hours.

The degree of relief obtained with the drug in each group is as follows:

GROUP 1: Of 10 patients with nausea but not vomiting, 7 obtained complete, 2 partial, and 1 no relief. Eight of 11 patients with nausea and vomiting obtained complete relief from both and one from vomiting only. Two remained the same.

GROUP 2: Five of 7 patients with nausea experienced complete relief and 2 partial relief. Three of 4 patients with both symptoms experienced complete and one partial relief.

GROUP 3: Two of 4 patients with nausea had complete relief, 1 partial and 1 none. Of 8 patients having both nausea and vomiting, 5 were completely relieved from both, 1 from vomiting only and 2 were unchanged.

GROUP 4: Seven of 10 patients with nausea had complete relief, 2 partial and 1 remained unchanged. Of 8 patients who had both symptoms, 4 obtained complete relief of both, 2 of vomiting and 2 had a decrease in the severity of both symptoms. One patient had severe emesis but did not complain of nausea; after treatment both symptoms were worse.

A total of 41 patients (65.1%) obtained complete relief of nausea

and/or vomiting; 16 (25.4%) obtained partial relief; and 6 (9.5%) were unimproved or worse. In one case of worsening, this was not attributable to the medication but rather to the course of the disease. Prior to medication with trimethobenzamide a total of 41 patients showed marked nausea and 14 marked vomiting, while following this medication 4 showed marked nausea and 2 marked vomiting.

No drowsiness, analgesia, tachycardia, skin rash or other side effects were reported by the patients nor noted by the professional personnel.

Discussion

Judged by effectiveness of response, these results with trimethobenzamide in treating nausea and vomiting in patients with neoplasms in conjunction with radiation therapy compare favorably with those of other investigators who have used Benadryl, Dramamine and Thorazine.[2] While other antiemetics reportedly produce side effects in 20 to 75 per cent of cases,[2] none were observed with trimethobenzamide. Drowsiness commonly occurring with other antiemetic agents does not occur, so that the drug can be prescribed without reservations except for the precautions usually followed when introducing any new agent into a patient's therapeutic schedule.

Rapid onset and relatively brief span of action of trimethobenzamide are also advantageous, the latter permitting the physician to make frequent observations in cases where other conditions may be masked by an antiemetic. Because of its low toxicity and convenient capsule form it can be given on an "as required" basis.

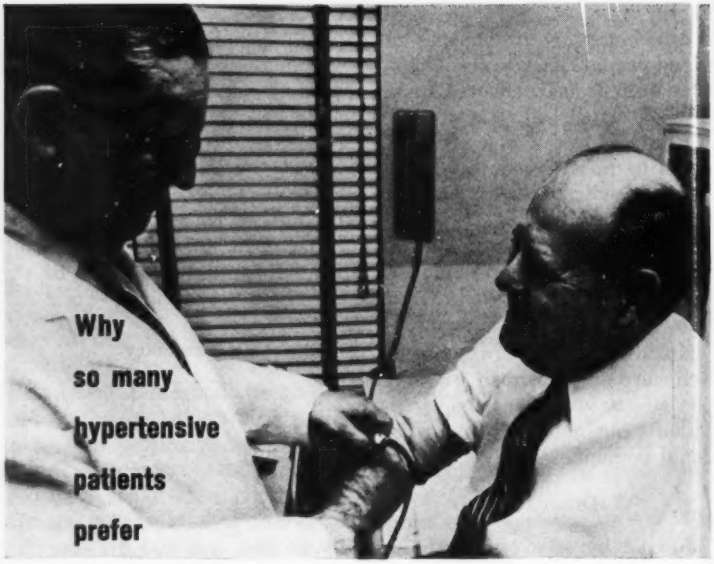
Summary

Trimethobenzamide was administered to 63 patients with nausea and vomiting during or following x-ray therapy. Except in patients with widespread disease, who were given 800 mg., the usual dose was 600 mg. per day orally.

Forty-one patients (65.1%) obtained complete relief of nausea and/or vomiting, 16 (25.4%) obtained partial relief, and 6 (9.5%) were unimproved. Onset of relief varied between 30 and 60 minutes with a duration of 3 to 4 hours. No side effects of any kind were noted.

Conclusion

Trimethobenzamide (Tigan) appears to be an entirely safe, effective antinauseant and antiemetic when used in conjunction with x-ray therapy in patients with neoplasms.◀



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*Herrmann, G. R., Vogelpohl, E. B., Hejtmancik, M. R., and Wright, J. C.: J.A.M.A. 169:1609 (April 4) 1959.

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Principles of Office Surgery

DAVID K. HEYDINGER, M.D., *Columbus, Ohio*

► *Disorders which can be safely treated by surgery in the office include certain pigmented nevi, verruca vulgaris, papillomata, some senile keratoses, sebaceous cysts, and abscesses, and superficial lacerations of the skin and subcutaneous tissues. Tetanus prophylaxis is required with lacerations.* ◄

There is much disagreement as to what surgery can safely be done in the physician's office. The physician must be his own judge as to the adequacy of his skill, knowledge, equipment and personnel to perform the surgical procedure and to deal with possible immediate operative complications.

Excision of Skin and Skin Appendage Lesions

This includes such lesions as certain pigmented nevi, verruca vulgaris, papillomata, some senile keratoses, and some sebaceous cysts. It is doubtful that sebaceous cysts of the face (especially the cheeks) should be an office procedure, for these often are so deep, surrounded by active inflammation, and contiguous to vessels, nerves and ducts of major importance, that excision can be a tedious and complicated procedure.

Any lesion that is worth excising is certainly worth examining under the microscope. If, for no other reason, the legal implications demand that microscopic examination be made of all excised tissue.

The patient with the small skin lesion is always placed supine or prone on the table (never sitting). The area cleansed with pHisoHex and aqueous zephiran, local anesthesia obtained with 1% Xylocaine or 1% novocain—using first a 25- to 27-gauge needle. After excision of the usual skin lesion (nevi, warts, etc.) direct ligature of vessels is rarely indicated. A fine scar and adequate hemostasis can be obtained with vertical mattress sutures of fine silk (4-0 or 5-0). Several minutes of direct pressure over the wound will prevent postoperative oozing. Sutures may be placed close together and tied

firmly on the face, scalp, neck or hands, because of the abundant blood supply in these areas. Because of the less abundant blood supply on any other area of the body, sutures there must be placed farther apart, farther back from the skin edge, and approximated loosely to prevent necrosis.

When excising sebaceous cysts, the same procedure is followed except that a small elliptical portion of skin is excised with the cyst so as to include the obstructed duct of the sebaceous gland. This helps prevent rupture of the cyst. When the yellow cyst wall is encountered, blunt dissection with small curved scissors will usually enucleate the cyst easily without rupture. No attempt should be made to excise a sebaceous cyst involved in an acute inflammatory process. Dissection through any tissue involved in an acute inflammatory process assumes the risk of a severe postoperative cellulitis (unless draining an abscess).

A Bartholin cyst should never be excised as an office procedure. Excessive bleeding can cause serious trouble.

Biopsies

Biopsy of a skin or mucous membrane lesion may often be an office procedure. After adequate cleansing and local anesthesia a small "sliver" (triangular piece) of the lesion and adjacent normal skin or mucous membrane is excised. Often, closure of the area is not necessary. If closure of a biopsy of mucous membrane (mouth) is necessary, fine chromic catgut should be used, to be removed in four days. If this type suture should come out and be carried into the tracheo-bronchial tree, it does not carry the risk of a non-absorbable suture such as silk.

Abscesses

Many small, superficial abscesses can be incised and drained in the office. After cleansing the area, enough 1% novocain (or Xylocaine) is placed in the thin skin overlying the center of the fluctuant area with a 27-gauge needle to blanch only the proposed incision site. Usually a ¼ inch edge of a 2 inch x 2 inch gauze square is cut, leaving one end attached to the gauze square. This small, attached portion of the gauze square is used as the drain and the gauze square is placed directly over the abscess and held in place with a small piece of tape. A larger gauze pad is placed over this. If sterile soaks are to be used, the larger, outer gauze square may be removed and the soaks applied to a relatively clean dressing. Also, if the patient fails to return, the drain automatically comes out when the dressing is removed.

If the abscess being drained is

from a foreign body, or if a foreign body previously incurred is being removed, tetanus antitoxin should be given (5,000 units to an adult), or a booster dosage of tetanus toxoid if the patient has been previously immunized.

Paronychia

This common infection (abscess) can be properly handled only by adequate drainage. Basal finger block anesthesia with 1% Xylocaine or 1% novocain is done. Since the abscess is beneath the proximal portion of the nail, this area must be drained, best by removing the proximal ⅓ of the nail rather than attempting to place a drain. Any incision in the skin (even with recovery of pus), without removal of the proximal corner or proximal ⅓ of the nail, is often inadequate.

Lacerations

This includes *only* the care of superficial lacerations of skin and subcutaneous tissue. Tetanus prophylaxis should be used in all lacerations unless an adequate reason can be given (in writing on the patient's record) for not using such prophylaxis. The suturing of lacerations should be the same as after excision of skin lesions. The physician, wearing gloves and mask, should cleanse the area with pHisoHex and aqueous zephiran, irrigate with saline, debride the wound, then re-irrigate with saline. If this routine is carefully followed with every laceration prior to suturing, antibiotics will seldom be needed and complications will be rare. If every laceration could have the edges completely excised under sterile technique, a dirty wound would be converted to a surgically clean one and results would be much improved. Debridement of lacerations of the face and hands must be minimal, but this, too, can be easily accomplished, using small plastic scissors and removing only a very small "sliver" along the whole length of the edges of the laceration.◀

Hematologic Changes After Total Gastrectomy

Of 59 patients with cancer of the stomach undergoing total gastrectomy, 40 survived from 1 to 4 years. All have required special care because metabolic and grave hematologic changes may progress from hypochromic to megalocytic anemia, to true pernicious anemia. Every patient surviving total gastrectomy for 3 years should have peripheral and bone marrow blood picture determinations made every 3 months.

Kothe, W., *Beitr. klin. Chir.*, 197:184-191, 1958.

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Management of Chronic Ulcerative Colitis

ROBERT A. SCHNEIDER, M.D.,* *Oklahoma City, Oklahoma*

▶*The protean factors influencing the course of chronic ulcerative colitis require that the patient be treated in a comprehensive manner. Although medical management is preferred, 10 to 35 per cent require surgery. An unsatisfactory doctor-patient relationship may be a primary factor in treatment failure.*◀

The satisfactory management of the patient with chronic ulcerative colitis remains a problem. However, advances in treatment including modern management of fluid and electrolyte imbalance, better surgical procedures and anesthesia, together with a better realization of the role played by psychological factors, have improved the outlook for these patients.

The best therapeutic results appear to be obtained by those general physicians or internists who will sustain interest in these patients and who have kept up with advances in knowledge of rational medical, psychological and surgical measures.

*Associate Professor, Departments of Medicine, Psychiatry, Neurology, and the Behavioral Sciences, University of Oklahoma Medical Center.

Clinical Picture and Course

Ulcerative colitis, one of the commonest of the serious disorders of the colon, is seen most often in young adults, may be of insidious onset, or may begin as a fulminating disorder requiring emergency treatment. In some patients the process affects only a portion of the colon and the patient remains ambulatory and fairly active. In others it becomes rapidly widespread and has major systemic complications. The average patient presents complaints of frequent watery stools with varing admixture of blood, pus, and mucus, abdominal cramps and tenesmus. Diarrhea is not a feature of every case. When the disease is localized to the rectum, the chief complaints may be of constipation and the passage of bright red blood. In the severe case, marked anorexia leads to signs of malnutrition and weight loss. Negative nitrogen balance is

usual, this due to deficient intake of protein and its excessive loss in the stool. There is a varying degree of anemia, in many cases fever, at times related to secondary infection in the colon or elsewhere. The clinical course can be followed by plotting day to day the number and character of the stools, weight, hemoglobin level, and temperature. In remissions, the stools are fewer, the temperature normal or slightly above, and the weight and hemoglobin levels rise. The diagnosis is made from the history, and by local sigmoidscopic and barium-enema x-ray examinations. On inspection, the colonic membrane shows a "nutmeg" appearing granular membrane in which are interspersed small punched-out ulcerations, at times confluent, leading to larger areas denuded of mucous membrane. The membrane is extremely friable and bleeds easily. Considerable spasm is noted at times interfering with passage of the instrument. The barium outlined colon is seen to be foreshortened, and to have a smooth "lead pipe" appearance, some areas showing the "saw tooth" appearance of multiple small ulcerations. Patients who are neglected may develop abscesses and fistulous tracts which may open onto the perineum or anterior abdominal wall.

Occasionally one sees various skin disorders, including a necrotizing type of skin ulceration, a rheumatoid-like arthritis or uveitis. Such complications suggest that this is a widespread disease not limited to the colon. In some patients with severe long-standing disease a degree of hepatic and renal failure ensues. In dealing with these patients, one is impressed by their emotional disturbance. Although a distressing chronic illness of this sort may lead to emotional disturbances, there is an accumulating body of evidence suggesting that the personality, attitudes and emotions of these patients contribute both to the onset and to the course. Time and time again, the onset or an exacerbation coincides with events such as going away to school, leaving home for the first time, a new job, marriage, birth of a baby, or when there have been interruptions in close relationships, such as between patient and mother, or patient and spouse. These patients appear to have certain features in common, such as passive dependency and immaturity, with considerable hostility which is poorly handled and rarely overtly expressed in action. Some consider the diarrhea to be an expression of a regression or return to a dependent, childlike situation; others that the frequent bowel movements are a disguised expression of hostility and that improvement occurs when the patient adjusts in a

more mature fashion, and vents his hostility in a more revealing manner or when he is able to gain some insight into the situation which has engendered so much unexpressed hostility. Successful management appears to entail an appreciation for the medical, surgical, and psychological aspects of this distressing disorder.

Theories of Pathogenesis

The precise pathogenesis of ulcerative colitis is unknown. We note involvement not only of the colon, but of the skin, eyes, joints, liver and kidneys, and development of hemorrhage, malignant change, fistulae, negative nitrogen balance, weight loss, fever, and "toxemia". The majority of these patients have difficulties of adjustment to persons about them and to responsibilities generally. Thus, it would appear that any theory of etiology must include a consideration of the total person.

Over the years, various microorganisms have been isolated from these patients suggesting that the disorder is primarily an infection of the colon.[1,2] Koch's postulates have never been fulfilled, and any infection present must represent secondary invasion. Allergy has never been demonstrated to play an important role. Some have considered this disease to represent a deficiency disorder involving protein, vitamins, and even deficiency of secretions from the wall of the colon. However, the correction of such deficiencies has not proven to be basically effective. Investigators have suggested that the ulceration in the colon might be due either to the proteolytic action of enzymes,[3] or to the mucus-dissolving action of lysozyme.[4] Increased amounts of these enzymes have not been demonstrated to be causatively related. The underlining disturbance has been thought by some to be dysfunction in the autonomic innervation of the colon. This led to the use of vagotomy[5] and presacral neurectomy,[6] with little lasting effect.

The widespread nature of the disorder including the involvement of joints, skin, and uveal tract together with the initiation of remissions by the use of ACTH and cortisone has suggested the possibility that the disorder might be a derangement of collagen tissue. The pathways or mechanisms by which the psychological disturbance could contribute to the pathogenesis of colitis, remain obscure.

Grace et al,[7] as a result of ex-

1. Bargen, J. A., *J.A.M.A.*, 83:332,1924.
2. Dragstedt, L. R., et al., *Ann. Surg.*, 114: 653,1941.
3. Ivy, J. H., & Clark, B. G., *Gastroenterology* 5:416,1945.
4. Meyer, K., et al., *Am. J. Med.*, 5:482,1948.
5. Dennis, C., et al., *Ann. Surg.*, 128:479,1948.
6. Hinton, J. W., & Shafiroff, B. G., The Human Colon, Paul B. Hoeber, New York, 1958, pp. 199.
7. Grace, W. J., et al., The Human Colon, Paul B. Hoeber, New York, 1951.

tensive study of exteriorized colons in patients with ulcerative colitis, conclude that colonic hyperfunction is the mechanism of basic importance in ulcerative colitis in man, and they consider this disorder to be a specific reaction to a number of influences which can initiate motor overactivity, chief among which are distressful life situations and sustained emotional conflict. Together with the increased motor activity, they have demonstrated engorgement of the mucosa, submucosal bleeding, and increased fragility of the membrane, such that small erosions may extend to ulceration and hemorrhage. They feel that the disorder is a result of colonic hyperfunction resulting from stress, leading to ulceration and hemorrhage, complicated by such factors as infection and protein loss. The concept that ulcerative colitis is a stress disorder is attractive and there now appears to be considerable clinical and experimental evidence to support it. A comprehensive approach to these patients with this broad concept in mind seemingly has improved our therapeutic efforts.

Medical Management

Although elective or emergency surgery may be required in the occasional patient, medical management is to be preferred in the majority of instances. This is largely symptomatic and corrective of any deficiencies. Water, sodium chloride, potassium, and magnesium deficiences must be detected and corrected. The anemia may require blood transfusions, and correction of the anemia may lead to considerable general improvement. Iron may also be administered by mouth if tolerated. Vitamins may be given either by mouth or parenterally. The nutritional deficiency poses a problem since the patient invariably is anorexic. It has been the custom to offer these patients a low-residue diet. We prefer a general diet and allow the patient to make his own selections. The patient unable to take sufficient food by mouth may have, by mouth or by nasal gastric tube, a mixture of protein hydrolysate (50%) and carbohydrate such as Dextri-Maltose (50%), 200 to 400 cc. every 2 hours while awake. Tube feeding may initiate or increase diarrhea if the solution is given too rapidly. Chemotherapeutic agents do not materially alter the course of the disease, and are best limited to those patients who have suppurative complications, such as pyoderma.

ACTH and cortisone occasionally may cause a dramatic remission but they have no curative power, and their injudicious use may lead to perforation, and the patient may relapse if the dosage is not properly tapered off. Furthermore, a degree of resistance to these agents may ensue such

that their effectiveness is reduced when they are reinstituted at a later date. These hormones should probably be reserved for the patient with fulminating and rapidly deteriorating disease.

The symptomatic control of the diarrhea presents a problem. Occasionally it is necessary to administer tincture of opium, but this must be done with caution because of the possibility of addiction. A barbiturate may be used to lessen anxiety and apprehension.

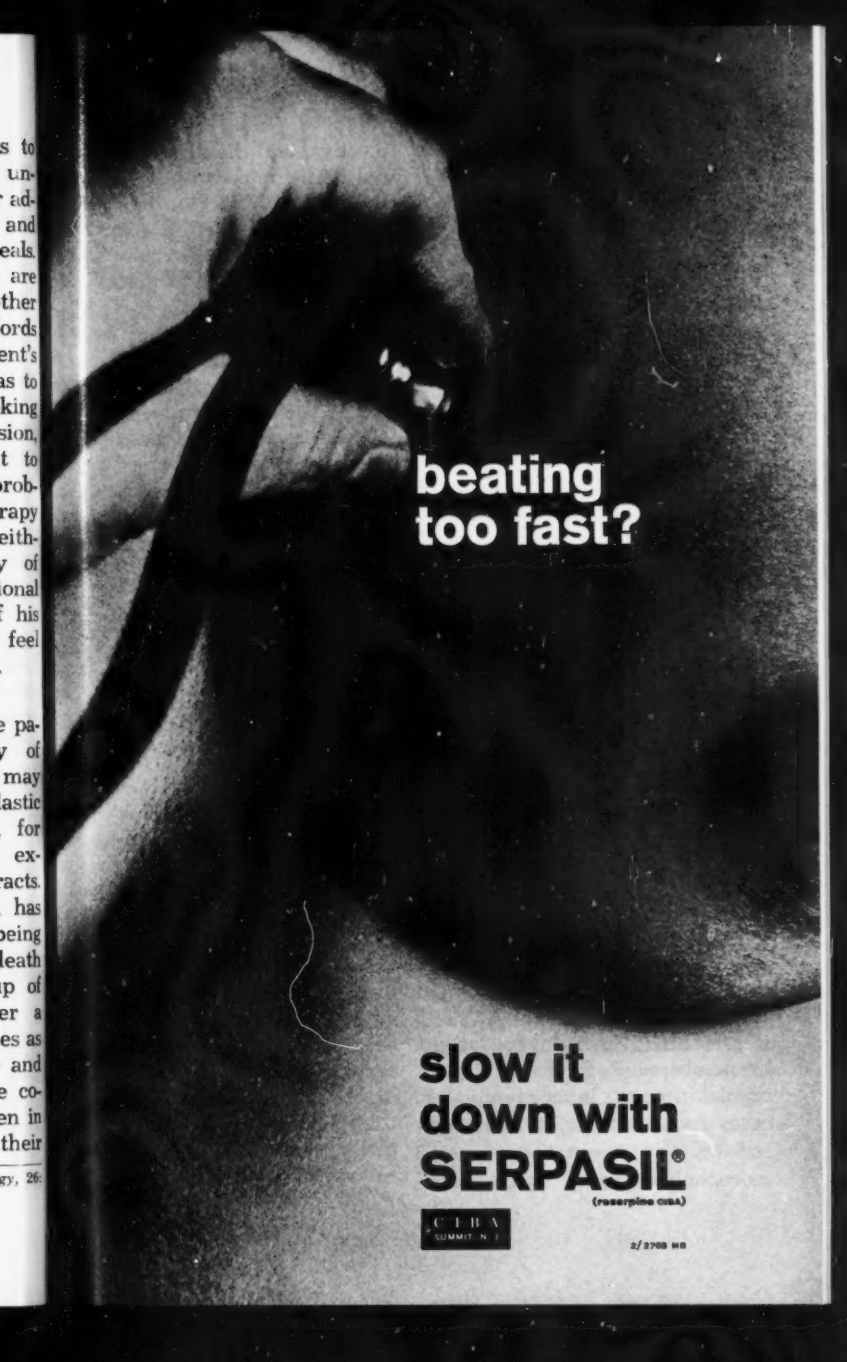
Psychiatric Aspects of Management

It has been shown repeatedly that the physician who has the general management of the patient is in the best position to deal with the psychological aspects. He need not be especially trained in psychiatry to do this adequately. Indeed too vigorous "probing" in an attempt to uncover conflicts has proved to be unwise, and to make the patient worse. Psychotherapy here hinges chiefly on the establishment of a successful doctor-patient relationship. These patients find it difficult to discuss their problems. For this reason, the psychotherapy is most successful when it is kept on a superficial level. Most successful is the physician who is friendly, consistent, and reliable, and is a good listener. Careful attention should be paid to even the most trifling aspects as they develop. The physician's aim is to get the patient better able to understand himself and to better adjust toward life in general and the people with whom he deals. Support and encouragement are essential. Often talk with other members of the family affords further insight into the patient's problems and possible clues as to improvements in therapy looking not only to inducing a remission, but to enabling the patient to solve adequately emotional problems of the future. Psychotherapy is not always successful due either to the rigid personality of some patients or to an occasional physician who, by reason of his own personality is unable to feel comfortable with the patient.

Surgical Management

Ten to 35 per cent of these patients will require surgery of some type. Elective surgery may be necessary should neoplastic change occur in the colon, for persistent polyposis, or for excision of fistulae or sinus tracts. The incidence of carcinoma has been variously reported as being 3.2 to 25 per cent.[8] The death rate from cancer in a group of these patients followed over a period of 19 years was 30 times as high as in a comparable age and sex group who did not have colitis. Carcinoma is chiefly seen in those patients who have had their

8. Bargen, J. A., et al., *Gastroenterology*, 26: 32,1954.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disease for 5 years or more. The incidence correlates to some extent with the presence of pseudopolyps, even though these polyps may recede and disappear in many patients who enter into remissions. Patients who develop pseudopolyps deserve, therefore, careful follow-up and biopsy when indicated.

The best type of definitive surgery now appears to be a one-stage procedure with ileostomy, total colectomy, and resection of the rectum. The postoperative mortality rate is low in good hands because of improved techniques, good anesthesia, and better care of nutritional and electrolyte balance. Colectomy may be an emergency procedure when perforation or massive hemorrhage occurs. In most cases it is elective, and the decision is made only after one carefully balances the advantages to be gained against the decided disadvantages of a permanent ileostomy. Perhaps a reasonable indication for colectomy is failure of the patient to improve after a fair trial of good medical management.

Conclusion

The patient with ulcerative colitis is best managed by the general physician or internist who is genuinely interested in these patients and aware of the advantages and the limitations of the medical, psychiatric and surgical aspects of treatment. In our experience, more failures in management have been due to inability of the doctor and patient to relate satisfactorily than to any one other single factor.◄

Spontaneous Cerebrospinal Rhinorrhea and Otorrhea

Leakage of cerebrospinal fluid through the nose and/or ear in a case of basilar skull fracture is usually recognized promptly and treated appropriately. When without trauma a clear, colorless fluid begins to escape through the nose or ear, a diagnostic problem is presented. Such discharge has been observed following intracranial tumors, in a number of cases spontaneously, at times associated with spontaneous pneumocephalus. Some cases have been treated surgically. Suggested possible pathways for escape of fluid in cases of spontaneous cerebrospinal rhinorrhea are: persistence of fetal craniopharyngeal canal; persistence of lumen of the olfactory bulb, with fistulous opening along the olfactory nerves or their sheaths; congenital defects in the cribriform plate with arachnoid extensions along olfactory nerve fibres. The latter is the most likely.

Mosberg, W. H., Jr., *Maryland M.J.*, 8:62-65, 1959.

Allantoin-Sulfonamide-9 Aminoacridine in Vaginal Suppositories to Prevent Postpartum Cervical Erosions

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►*Early treatment of cervical erosion and the resulting infection following postpartum should consist of an easily administered medication that is convenient for the patient. In this study among 25 prima- and multigravida patients 60 per cent had a reduction in endocervicitis following the use of this preparation.*◄

The Cervix Uteri a Vulnerable Part

The cervix is vulnerable to injury during parturition and in spite of excellent obstetrical procedures, the incidence of injury remains high. The injury may be a minute nick in the mucosa or a deep rent extending throughout the cervix. Erosions and hypertrophy of the cervix are frequent and are associated in many instances with endocervicitis.

Hippocrates[1] in his Prognostics stated that "Ulcerations in the womb from parturition, an abscess of a chronic nature, or from any other cause, is necessarily accompanied with fever, buboes and pains in the place; and if the lochial discharge be also suppressed, all these evils are more intense and inveterate, along with pains of the hypochondrium and head. And when the ulcer heals, the part is necessarily smoother and harder, and the woman is less adapted for conception."

Erosion of the cervix is characterized by a red granular area surrounding the external os, due to maceration and desquamation of the squamous epithelium, and the covering of the denuded area by cylindric ciliated epithelium which grows from the cervical cord. The cervical discharge is most frequently stringy, glairy, viscid, thick, tenacious and mucoid, but may at times be mucopurulent.

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1. Adams, F., Genuine Works of Hippocrates: On the Prognostics. William Wood & Co., New York, 1:220,1926.

The Earlier the Treatment the Better

The treatment of these postpartum conditions must be immediate and adequate so as to reduce more serious consequences which might result from neglect. The successful treatment of cervicitis—which in many cases is a predisposing and perpetuating factor—will frequently result in healing of the erosion. The treatment of the described postpartum problem should be simple and easy so that the cooperation of the patient is assured. It should, as Angelucci[2] pointed out, "fulfill the therapeutic objective set forth by the Council, of 'thoroughness and persistence with the simplest and least messy procedure'."

When several methods of treatment are available, utilizing the same therapeutic agent, and positive clinical results are obtained, the treatment requiring the least effort on the part of the patient should be the one of choice. A vaginal cream containing allatoin 2%, sulfanilamide 15% and 9 aminoacridine 0.2% in a watermiscible base adjusted to an acid pH has been used with good to excellent results. Since this cream had to be inserted by means of an applicator, some patients raised objections to its use. To eliminate the objection to the use of a applicator, the same formula wa made available in a glycerinated gelatin capsule for evaluation.

A controlled study was de signed to evaluate the effect o the allantoin, sulfanilamide, aminoacridine suppository* o cervical erosions, vaginal dis charge and infection in the post partum patient.

Materials and Method

In a series of 50 patients, th odd numbered ones were selecte for treatment with the suppos tories, and the even numbere used as controls. In the treate group there were 11 primigravi das and 14 multigravidas, in th control group 12 primigravida and 13 multigravidas. Bacterio logic studies were made in both groups on the first and fifth post partum days. Three types of me dia were used: blood agar plate for identification of bacteria Nicherson's medium for fungi and an enriched broth to cultur Trichomonas vaginalis.

Patients of the two groups were hospitalized for five day postpartum and treatment ca ried out as described.

1. The AVC Suppository treat ed group: Starting with the firs postpartum day until the day o discharge from the hospital, th

2. Angelucci, H. M., *Am. J. Obst. & Gynec.*, 50:336-338,1945.

*AVC® *Suppository*, National Drug Co., Phil delphia, Pa.

nurse inserted a suppository high up into the patient's vagina, morning and evening. The patient was instructed to remain on her back for at least one hour following each insertion of a suppository. Suppository treatment was terminated when patient left the hospital.

2. The control group was treated by the usual accepted methods of postpartum hygiene and care.

Follow-up examinations were made in a majority of the patients six weeks postpartum.

Results

Of the 25 suppository-treated patients, 13 patients had clean cervices; 4 showed a slight erosion and 3 required treatment of erosion. There were 5 patients who failed to return for a follow-up check.

In the patients requiring further treatment the cervices were cauterized and treated with AVC Suppositories twice daily for 10 days resulting in a complete disappearance of the lesion.

Of the 25 patients in the control patients, 8 patients had clean cervices, 10 showed slight erosion and 5 required treatment of erosion. Two patients failed to return for follow-up check.

In the five patients requiring further treatment, the erosions were cauterized and treated with AVC Suppositories inserted high up into the vagina twice daily for 10 days. One of these patients had to be treated for an additional 10 days to effect a satisfactory clinical result.

The bacteriologic studies of the fifth postpartum day compared with those of the first portpartum day showed a significant control and reduction of bacterial growth in the treated (AVC Suppository) group; in the control group there was an increase in mixed infections, particularly in the number of staphylococcic and non-hemolytic streptococcic infections.

Discussion

Following a clinical trial of a formula containing allantoin 2%, sulfanilamide 15% and lactose 5% in a special greaseless base buffered to a pH of 4.5 with lactic acid, it was reported that it presented a convenient and rapid method of treating Trich. vaginalis vaginitis.[3] Furthermore, the gratifying results obtained with the treatment recommended it as a convenient and effective method of treating many ulcerative lesions of the lower genital tract of the female.

It has been found that treatment of the cauterized cervix with application of allantoin-sulfanilamide-lactose cream twice daily reduced healing time on the

3. Parks, J., *M. Ann. District of Columbia*, 12: 175,1943.

average of one half compared to previous accepted methods of treatment.[4,5] The pain was usually controlled and the patients commented on the comfort afforded by the use of this cream.

In a series of severe chronic cervicitis treated by conization of the cervix, an improved formula containing allantoin-sulfanilamide-9 aminoacridine was used to:

1. Reduce the incidence of infection.
2. Prevent acute flareups after conization.
3. Stimulate healing.
4. Reduce sloughing.

Most patients were healed in 2 weeks and all in 4 weeks. In no case was there a resulting stenosis. The usual sloughing discharge was greatly reduced.[6]

4. Horoschak, A., & Horoschak, S., *J.M. Soc. New Jersey*, 43:92-95,1946.
5. Horoschak, A., & Horoschak, S., *Revista Cubana, d Obst. & Gynec.*, 9:105-111,1947.
6. Hensel, H. A., *Postgrad. Med.*, 8:293-296, 1950.

The results observed in this study establish the effectiveness of allantoin-sulfanilamide-9 aminoacridine supplied in glycerinated gelatin suppositories in the treatment of postpartum cervical lacerations and erosions. These suppositories, used as described, modified the vaginal debris so that freer drainage was established and healing was accelerated.

Conclusion

The incidence of postpartum cervical erosions was reduced about 60 per cent with the use of allantoin-sulfanilamide-9 aminoacridine in glycerinated gelatin suppositories. Results of bacteriologic studies suggest that endocervicitis can be successfully treated with these suppositories. The suppositories are easy to use, non-irritating and effective, and have good patient acceptance.◀

Simple Regional Nerve Block For Surgery of the Hand and Forearm

The procedure involves injection of 10-12 ml. of 0.2% lidocaine solution with a 1:200,000 dilution of epinephrine near the brachial artery. The patient lies flat on his back with the forearm placed flat on the table and the elbow flexed at 90°. With one hand the operator palpates the brachial artery just distal to the pectoralis major tendon. The needle is inserted through the fascia and then tipped to barely miss the branchial artery. If no blood appears when the plunger is partially withdrawn, 8 ml. of solution is deposited as the needle is moved in and out over ½ in range of the neurovascular space.

Burnham, P. J., *J.A.M.A.*, 169:941-943,1959.

Some of the Advantages of Cobalt-60 Teletherapy

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CHESTER A. STAYTON, JR., M.D.,* *Indianapolis, Indiana*

► *The improved tumor doses possible with the Theratron Junior cobalt-60 therapy unit afford a new advance in the treatment of various types of malignant tumor. Improved patient tolerance and operator convenience were noted after treatment of more than 200 patients with this method.* ◄

Cobalt-60 teletherapy is a form of external irradiation therapy. It functions by the emission of homogenous gamma rays of 1.17 and 1.33 million volts from a small artificially-prepared radioactive source. These rays produce biological effects similar to the effects of the spectra of x-rays emitted from generators of two to three million volts. Cobalt teletherapy is useful as a deeply-penetrating form of irradiation therapy primarily for the treatment of malignant tumors.

The clinical advantages of cobalt-60 teletherapy have been well defined. There is an unusually high degree of skin tolerance since the skin dose is only 20 to 40 per cent of the air dose, and the maximum or 100 per cent dose is delivered 5.0 mm. below the surface. This feature permits much larger doses through single portals and, in some instances, retreatment of previously irradiated areas. The skin effect is less than that found in million-volt therapy, and it appears to be less than the effect found with some higher voltage x-ray generators as well. The second advantage of cobalt-60 teletherapy is a lower incidence if irradiation sickness. This is attributed to a well-defined beam with less lateral scatter and a diminished volume dose. The clinical result is an improved tumor dose without interruption of treatment due to irradiation sickness. The third advantage of cobalt-60 teletherapy is an increased depth dose. This results in improved tumor dose

*From the Department of Radiology, St. Francis Hospital, Beech Grove, Ind.

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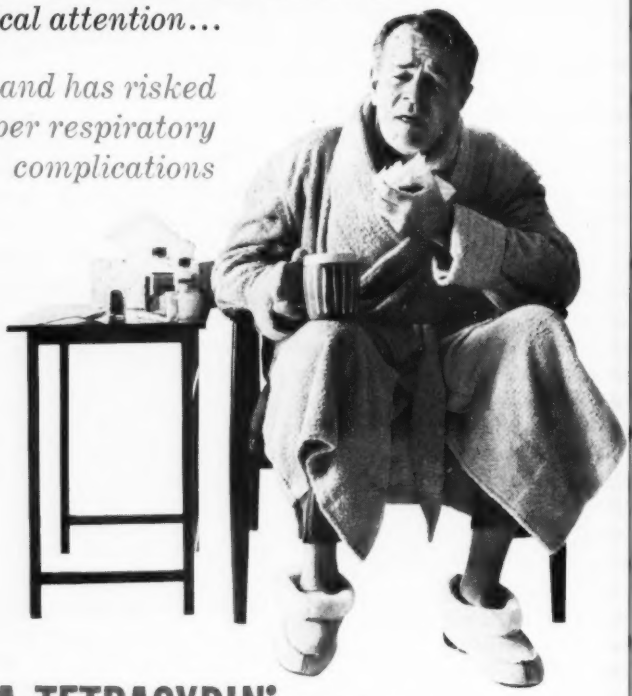

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in the same number of treatments, or similar tumor dose with fewer treatments than with conventional x-ray. A fourth and very important advantage is the similar absorption of the rays in bone, cartilage, muscle and fat. The absorption coefficient is the same for all of these tissues. In the case of conventional therapy, there is at least twice as much absorption of irradiation dose in bone as there is in tumor of muscle density, and there is 1.5 to 2.0 times as much absorption in cartilage as there is in tumor tissue. The important clinical aspects of this feature of cobalt-60 teletherapy are:

1. A lack of chondritis following treatment of laryngeal lesions or treatments necessarily administered through the cartilage of the ear.

2. An apparent lack of hip fractures due to decrease in absorbed bone dose in patients treated for carcinoma of the cervix.

3. No injury to bone flaps in patients treated postoperatively for brain tumors.

In the calculation of tumor doses, no correction is necessary for irradiation absorbed in intervening bone or cartilage.

The treatment machine used in the management of these patients was a Theratron Junior rotational cobalt-60 therapy unit. With this unit, the patient is treated while recumbent, and the source may be rotated around him. The tremendous weight of the head is counterbalanced by the back shield. Precision setups are possible, and duplication of treatment fields day after day is a simple matter with this type of apparatus. Many types of rotational apparatus are in use and afford opportunities for improved treatment techniques. Rotational therapy should be regarded as the ultimate form of multiple portal therapy. Rotational therapy with the patient sitting on a revolving treatment chair can be accomplished with the "fixed-head" type of equipment, but precision centering and duplication of portals is not so easy as it is with the Theratron type of equipment. It is, of course, impossible to rotate the treatment head of large electrical generators in the 1-Mev to 2-Mev range. The patient must be rotated when this type equipment is used. The Theratron Junior appears to be a desirable instrument, capable of handling 40 or more patients daily.

This analysis is based upon early results in 300 patients treated for various types of malignant tumor by cobalt-60 teletherapy. No attempt is made to assess the end results in this group of patients, and such an evaluation will not be forthcoming for several years. There is little doubt that a more aggressive

and rewarding type of palliative therapy can be administered by cobalt-60 than is possible by conventional means, and it appears that local tumor control is improved as a function of increased dose. Improved end results may be anticipated in a few instances as a result of increased dose.

Carcinoma of the Lung

A large number of the early patients were suffering from carcinoma of the lung. While it is doubtful that any of the first patients with this disease has been cured by cobalt-60 teletherapy, there is no doubt that many have lived more comfortably and longer as a result of the improved tumor dose. Improved tumor dose can be achieved without losing sight of the important principle of palliative treatment, "Never make the treatment worse than the disease." Retreatment of patients with lung cancer, whose radiation tolerance has been exhausted by conventional x-ray therapy, has not been useful in this small group.

Head and Neck Carcinomas

It appears that patients with head and neck cancer can be treated more effectively with cobalt teletherapy than by conventional x-ray. Fewer portals need to be utilized, and unilateral disease can frequently be treated through a single lateral portal. For example, a patient with carcinoma of the tonsil with a metastatic node and a patient with carcinoma of the extrinsic larynx with metastatic nodal disease were treated in this fashion with good local tumor control and without ill effect. Midline carcinomas, such as those of the nasopharynx or sphenoid sinus, with or without metastatic nodal disease, can be best treated by two apposing portals. No injury to the bony structures or to the cartilages of the ear or larynx has been observed, and large tumor doses in the order of 6000 *r* in four to five weeks have been administered without ill effect. In this group of patients, we might anticipate slight improvement in end results by virtue of the ability to give larger doses.

Patients with residual glial tumors of the brain appear to have benefited by cobalt-60 teletherapy. These lesions are never well demarcated from normal brain tissue and, in most instances, the surgeon must be satisfied with incomplete removal of the tumor. Patients of this type can be treated promptly after surgery, usually with a single large lateral cobalt-60 portal, with no concern for the overlying skin or the bone flap through which the treatment is given. Tumor doses of 5000 to 6000 *r* in four to six weeks have been given with marked clinical improvement in the patient and

without apparent injury to the intervening tissues (except epilation). It does not appear likely that the cure rate in this group of patients will be improved by cobalt-60 teletherapy, but the early palliative result appears to be better. Exceptions to this were two patients with glial tumors of the brain stem who tolerated their treatment poorly due largely to brain-stem swelling and increased intracranial pressure. It is interesting to observe contralateral epilation occurring seven to ten days before epilation of the treated side in this group of patients.

Carcinoma of the Breast

In carcinoma of the breast, one must adopt an entirely new concept when he considers prophylactic postoperative therapy. Patients who were formerly given erythema and moist desquamation of the skin in an effort to obtain satisfactory dosage to the axilla, supraclavicular space and parasternal nodes by conventional means, can now be treated to far greater dosage levels without visible skin effect. The chest wall can be treated successfully through tangential portals so that a satisfactory dose can be administered to the entire tumor bed without producing disabling pulmonary fibrosis. We are no longer weighing the value of postoperative therapy against the hazards of postoperative treatment. We must consider postoperative therapy in the light of possible improved cure rate alone.

Carcinoma of the Uterine Cervix

The case for cobalt-60 teletherapy in treatment of carcinoma of the uterine cervix is a good one. When the actual dosage possible with conventional x-ray is surveyed, it is often found that despite the use of large pelvic portals the dose to Point B (lateral pelvic wall) is far short of that for which is aimed. Efforts to increase the dose at Point B, using conventional means, have been made utilizing transvaginal x ray. Dosages more in the order of those desired can be obtained, but it is virtually impossible to utilize a transvaginal cylinder larger than 3.5 cm. in diameter. Consequently, the areas covered by this treatment are small, and the x-rays may miss their target completely. When cobalt-60 teletherapy is used, adequate dosage to the lateral pelvic wall can always be achieved (3000 to 5000 *r* with cobalt plus radium dosage to 6000 *r* or more). We have been content with total dosage to Point B in the order of 5500 *r* contrasted with 3500 to 4500 *r* by conventional means (including radium). Of course, a more uniform dosage pattern is achieved by the utilization of apposing anterior and posterior cobalt-60 por-

tals than with conventional transvaginal x-ray portals.

Another indication for cobalt-60 teletherapy in carcinoma of the cervix appears to be in those instances where the first radium application was unsatisfactory. Patients with virginal introitus or with carcinoma of the cervical stump can be given rotational therapy, a so-called "pelvic bath" of irradiation to a cylinder 15.0 cm. in diameter and 15.0 cm. long, and second radium applications can be omitted. By combining transvaginal x-ray and rotational cobalt-60 teletherapy much more satisfactory doses can be obtained in stump cases.

"Pelvic bath"type of therapy is indicated in advanced carcinoma of the cervix and as postoperative treatment where it is known that residual tumor is present after the surgery. Those patients with Stage III and Stage IV lesions of the uterine cervix can be given 4000 to 4500 *r* by rotation therapy before evaluating their suitability for radium application. The most disappointing group of cervix patients treated with irradiation therapy by conventional means has been advanced cases where too aggressive treatment has been attempted combining radium and x-ray. If the lesion is sensitive to pelvic bath irradiation, the preliminary dose can always be supplemented with a later application of radium. If it is insensitive, no harm has been inflicted on the patient by the pelvic bath technique.

The final group of cervix patients for which cobalt-60 teletherapy rotation appears to be indicated is that group of Stage I and Stage II patients in whom primary radical surgery has been performed. We have given 4500 *r* to the 15.0x15.0 cm. pelvic cylinder in 30 days immediately postoperatively when the uterus has been removed and the iliac nodes dissected. The follow-up on three patients treated in this fashion has been short, and we are unable to predict late changes, but there are certainly no early untoward effects. Of course, this technique would require modification if ultraradical or excessively traumatizing surgery were performed. There is a great theoretical advantage in this form of treatment where the possibility of operative spread of tumor cells exists.

Genito-Urinary Carcinoma

Some lesions of the urinary tract appear to be best treated by cobalt-60 teletherapy. Infiltrative carcinoma of the urinary bladder can be well treated by rotation therapy, and localized large doses can be administered without injury to adjacent structures. Postoperative testicular tumors can be treated with cobalt-60 teletherapy as they can with other

form of supervoltage therapy, with a considerably lower incidence of irradiation sickness. In the past, it has been extremely difficult to treat seminoma postoperatively with adequate dosage by conventional means.

Summary

High-voltage irradiation therapy utilizing a cobalt-60 source has been discussed. After treating more than 300 cancer patients with cobalt teletherapy, certain advantages of this form of therapy over conventional x-ray therapy are evident. Improved patient tolerance and more convenience to the doctor are noted, particularly in the uterus, head and neck, breast and genito-urinary tract.◀

Relief of "Mass-Reflex" Spasm: Preliminary Clinical Report

Mass-reflex spasm appears first in the feet and lower legs. Its characteristics are:

1. An excessive, self-propagating maximal motor response to a minimal noxious sensory stimulus, most typical if applied to the soles or in the region of the ankles. The motion may be either pure flexor, pure extensor, alternate, or mixed.

2. Tendency to form a vicious circle as the result of repeated sensory stimuli which originate in the area of muscle and tendon contractions, and which in turn produce more muscle responses out of which arise more motor-producing sensory stimuli. If untreated this vicious circle can and will produce severe, uncorrectable damage.

3. The semi-isolated reaction, which involves in its own vicious circle the bladder, the external urethral sphincter, the rectum and the anal canal. This spasm has to be started as an integral part of the total mass-reflex skeletal-muscle spasm.

This is probably the first instance that the mass-reflex spasm associated with a partial spinal-cord injury has been treated and cured by procaine injections of a peripheral nerve. Three such patients have had their spasm treated by the method of procaine injection of the sciatic nerves for leg and body spasm, and by injection of the ulnar, median and radial nerves in both arms at the junction of the upper and middle thirds of the brachial arteries for arm and hand spasm. Selective anterior-rootlet rhizotomy may be indicated in certain cases.

Munro, D., & Spatz, E. L., *New England J. Med.*, 260:1-6,1959.

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Status of the Surgical Correction of Mitral Regurgitation

EARLE B. KAY, M.D.,* and H. A. ZIMMERMAN, M.D.,*
Cleveland, Ohio

► *With current surgical techniques, mitral valve regurgitation can be successfully treated in 85 per cent of patients. While precise techniques vary, direct vision is preferred over the closed method. Selection of patients depends on the degree of myocardial reserve and pathology within the valve.* ◄

Over 80 patients with mitral regurgitation have undergone surgery since 1951, employing various techniques. In nearly half of the cases closed techniques were used between 1951 and 1956. An occasional excellent result was obtained during this initial phase, but for the most part early enthusiasm for a particular closed technique was later dampened, success being either transitory or attained in only a small percentage of patients. It was evident that further progress would come only when the procedure could be carried out under direct vision. Since 1956 surgery was done on 45 patients with mitral regurgitation, employing the principles of direct vision correction. During this time there have been modifications and refinements of the techniques employed, including annular plication to decrease the size of the dilated mitral annulus, plastic procedures to regain valve motility, and valve substitution in the form of partial valve cusps. Today satisfactory correction can be achieved in 85 per cent of patients with mitral regurgitation. The valves of the remaining 15 per cent are so destroyed as to require complete replacement. Much work is being done in many research laboratories on this remaining problem, the solution of which seems not to be far in the future.

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Value of Open Method

A sufficient number of patients have now been operated upon by

the open technique, utilizing the mechanical pump oxygenator, to allow an appraisal of what can be accomplished, and crystallization of opinion as to what cardiac studies are indicated as well as the basis for selection of patients for surgery.

Cardiac Evaluation Studies and Selection of Patients

Prior to the development of an effective technique for surgical correction, much effort was directed at excluding patients with mitral regurgitation or multivalvular disease. Many diagnostic tests were employed to aid in this differentiation, including left-side cardiac catheterization, Evans Blue dye dilution cure and diodrast studies. Although these examinations in skilled hands are not likely to cause serious complications, they frequently exhausted the cardiac patient, and frequently failed to provide the desired information. The need for this more precise preoperative information is now less important, since the information can be readily obtained at the time of surgical exploration by pressure studies and direct examination.

The history of the clinical course and physical examination still remain very important features of the appraisal. The electrocardiogram and x-ray examinations give valuable information as to chamber hypertrophy and dilation. It is particularly valuable to have previous studies available for comparison to detect significant change of the disease. Phonocardiograms are employed for comparison with postoperative studies. Definite improvement in the valve sounds is now being seen—a very infrequent occurrence in patients operated upon with closed techniques. Right-side cardiac catheterization, with and without exercise, is routinely employed to determine the status of (and changes in) the pulmonary vasculature, and to obtain information on cardiac output and reserve. Pulmonary wedge pressure studies made at this time provide an index of left atrial pressures and suggestive evidence as to regurgitation, stenosis, or both.

It is important to investigate rheumatic activity by sedimentation rates, the presence of C-reactive proteins, and to have a period of hospital observation. Liver and kidney function tests are employed when indicated. A longer period of observation may be necessary to determine response to therapy.

If these studies show the symptomatic patient to have an enlarged heart, electrocardiographic evidence of left atrial and ventricular overloading, evidence of pulmonary hypertension aggravated by exercise, without signs of activity, operation is recommended. This is particularly so if

serial x-ray and electrocardiographic examinations reveal disease progression. Increase in the size of the cardiac silhouette, progressive shift of the electrical axis to the right, and aggravation of pulmonary hypertension are important leads to the need for surgical intervention. Once there is evidence of progression of these signs, however, it is considered to be unwise to postpone operation. Patients with enormous hearts, with or without evidence of failure, are advised to take long periods of bed rest in the hospital under constant, direct medical supervision to improve their myocardial reserve. Operation is delayed for optimum response to strict medical management.

The selection of patients for surgical correction is based upon results obtained. The two main factors in operative mortality, morbidity, and unfavorable results are insufficient myocardial reserve and pathology in the valve of such nature as to prevent hemodynamic improvement. Since there is now a successful method of surgical correction, surgical intervention should be recommended while the patient has the cardiorespiratory reserve adequate to withstand the procedure. In 15 per cent of patients the valve will be so destroyed that, with techniques now available, hemodynamic improvement will be insufficient for a favorable result. This group will require partial to complete valvular replacement with artificial valves. Two types of valves comprise this group:

1. The highly calcified, destroyed valve.

2. The highly scarred, immobile valve with matting and fixation of the cusps to the contracted papillary muscle, with absorption and loss of the chordae tendinae—impossible to detect preoperatively with any degree of certainty.

The highly calcified valve can easily be detected either with Bucky x-rays or by studying valve action under the image amplifier. Until satisfactory artificial valves for complete replacement are developed, operative intervention is being postponed in this latter group.

Analysis of Patients

There has been an operative mortality of 20 per cent in the first 45 patients operated on. This has varied from 10 per cent in patients with pure mitral regurgitation to 25 per cent in patients with combined mitral stenosis-mitral regurgitation. Three of the nine postoperative deaths were from air embolism. The factors contributing to this occurrence have been recognized, carefully studied in the research laboratory and now completely eliminated for the future. Two of these patients had grossly destroyed valves with

questionable hemodynamic improvement. Two patients died from insufficient myocardial reserve, the other four from insufficient hemodynamic improvement in cases of severely destroyed valves. Earlier operative intervention and the perfection of an artificial valve will materially reduce the mortality.

The effectiveness of correction, largely dependent upon the severity of the pathological process, improved with refinements in technique and increasing experience. Those patients with pure mitral regurgitation in whom there was adequate pliable valvular tissue were ideal candidates. These comprised 30 per cent of the series. The majority of the patients with combined mitral stenosis and regurgitation without complete destruction could also be benefitted. Those patients with severely destroyed valves (13%) for the most part were not benefitted.

Technique

A rotating disc oxygenator has been used in all such cases. The only major design change has been the use of convoluted discs that increase the oxygenating surface area by 40 per cent. The pumping mechanism developed by Pemco Company in Cleveland is now available in a large model, consisting of four pumps, one each for the arterial and venous line, a third for the sump return, and the fourth for use in direct coronary artery perfusion in cases of aortic valvular correction.

The surgical technique employed is varied with the presenting pathological features. The details of such techniques have been published elsewhere[1,2,3] and will not be repeated in detail. Patients with pure mitral regurgitation in whom the valve cusps and musculotendinous mechanism are good, and in whom the regurgitation is due primarily to a dilated annulus with separation of the valve cusps and some loss of valvular substance, can be effectively corrected by means of annular plication. It was found that sutures in and about the annulus had to be reinforced by small sections of compressed ivalon to prevent their tearing. Valves in patients with mitral stenosis *and* mitral regurgitation may be effectively corrected by first increasing the size of the orifice by commissurotomy, then by regaining valve motility by freeing the matted and fused cusps or chordae tendinae and papillary muscles, and last by correcting the insufficiency by means of either annular plication or by the addition of valvular tissue in the form of plastic material. The de-

1. Kay, E. B., et al., *Surg.*, 44:325,1958.
2. Kay, E. B., et al., *Am. J. Cardiology*, 2:281, 1958.
3. Kay, E. B., et al., *J. Thorac. Surg.*, 36:677, 1958.

stroyed valve necessitates valvular excision and replacement by partial or complete prosthesis. There is room for improvement in this latter technique. However, great strides are being made.

Hemodynamic Improvement

Pressure recordings of left atrial pressure obtained immediately prior to and following surgical correction were correlated with pulmonary artery pressures and lung biopsies to determine the degree of pulmonary vascular sclerosis as an aid to prognosis. There was an average left atrial pressure preoperatively of 36/16 mm. of Hg., postoperatively of 16/6 mm of Hg. The reduction in heart size and marked relief of symptoms all point to a gratifying result. Re-evaluation now, one to two years following correction, demonstrates that this correction is maintained. It is evident that with refinements in technique, greater improvement has been afforded the recent patients over those operated on early in the series.

Complications

There have been two types of postoperative complication in 15 per cent of the patients. The murmur recurred after a few of the early operations, due apparently to sutures pulling out. By reinforcing the sutures so that the tension is against the incorporated sections of ivalon, this complication appears to have been eliminated. The other complication is a febrile episode due either to a subacute bacterial endocarditis, (all blood cultures have been negative) or to an exacerbation of rheumatic activity which may have altered what initially appeared to be a good result. This has led to the use of larger dosages of broad spectrum antibiotics for a longer period of time during convalescence, with what appears to be a satisfactory reduction in the frequency of such episodes. Steroid therapy when indicated is also used postoperatively. This syndrome is also found following the "closed commissurotomy" technique for mitral stenosis.

Valvular Prosthesis

Much research has been done during the past two years on partial and complete prostheses for valve substitution and replacement in patients with varying degrees of valve destruction. Prerequisites for a permanent valve are:

1. It must not be toxic to the tissues nor cause any undue tissue reaction.
2. It must be of material that is not affected by the body electrolytes.
3. It must not cause destruction of red blood cells, platelets or fibrinolysis leading to bleeding tendencies.

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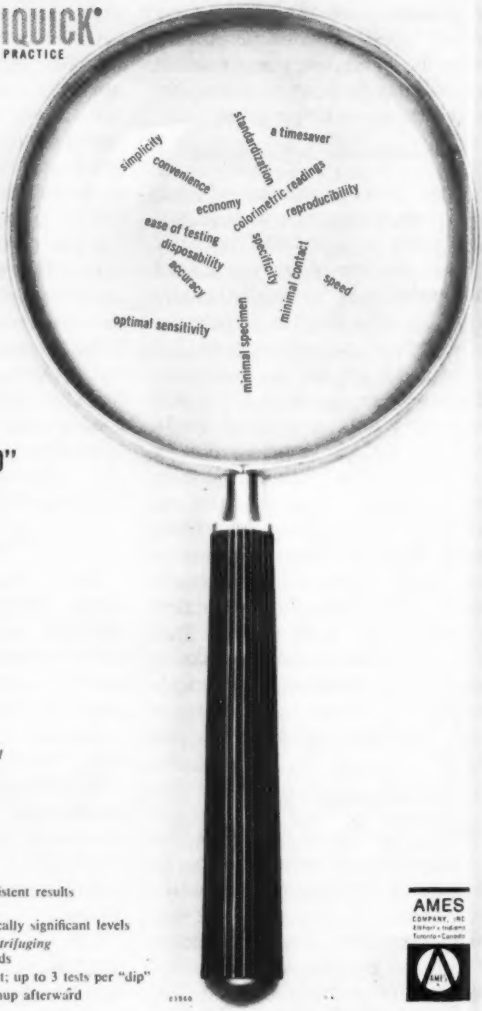

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4 It must not cause clot formation and embolization.

5 It must maintain optimal hemodynamic pressure-flow relationships.

6 Valvular tissue must remain pliable for a long period.

Porosity is advantageous so that it can be easily incorporated by the heart tissue and further strengthened by endothelium and tissue matrix. Ease and permanence of fixation are important considerations. Studies of valve design and construction have included comparative analyses of various plastics, the use and reaction of plasticizers for valve pliability, binding techniques between plastics with different physical properties, and fixation techniques. Valves have been fashioned and molded from the donors' own tissue (aortic and auricular wall). Recently a valve of new construction and material has been developed which appears to fulfill all of these requisites and to show the greatest promise for use in valvular replacement. This valve is still being tested and will be reported at a later date.

Mitral Stenosis

Good results from mitral commissurotomy have been reported in 50 to 75 per cent of the patients so treated, maintained in 50 per cent of the patients for up to five years. These data, coupled with the low operative mortality for the closed method of commissurotomy, present a fairly optimistic impression of the surgical treatment of mitral stenosis. These data, however, for the most part do not include all patients with highly calcified valves for which nothing could be done, those patients who were found to have associated mitral regurgitation, or an auricle so clotted that the surgeon feared to continue the procedure because of the danger of increasing the incompetence or of producing embolization. In some instances those patients with marked cardiac irritability or occasional arrest in whom the surgeon did not choose to persist in his efforts to obtain maximal enlargement were not included.

There has been an increasing number of reports recently concerning re-stenosis of the valve in 10 to 20 per cent of the patients, occurring within several years of the operative procedure. Re-activation of the rheumatic process accounts for perhaps five per cent of the re-stenosis. The opinion of most cardiac surgeons is that the valve was incompletely opened at the time of the operation. At least half of those recently polled[4] were dissatisfied with the results of the closed technique in the treatment of mitral stenosis in over 50 per cent of such patients. This agrees with our experience.

4. Report of Section on Cardiovascular Surgery of Am. College of Chest Physicians: to be published in *Dis. of Chest.*

For the past 18 months the pump oxygenator has been kept available for patients with mitral stenosis. In case the valve cannot be adequately opened by the closed technique, because of a clotted auricle, a highly calcified valve, or associated regurgitation, the necessary cannulations are made and the surgical correction performed under direct vision through the open heart. It is felt that this has considerably increased the number of patients benefitted, as well as the degree of benefit afforded each patient. Use of the pump oxygenator and extracorporeal perfusion has enabled the surgeon to support the circulation while performing the commissurotomy in those patients in whom the operative procedure would have been discontinued or incomplete because of hypotension, cardiac arrhythmias, or an occasional arrest. At least 85 per cent of the patients with mitral stenosis have as complete an operation as possible as compared to 50 per cent by the closed technique. This has reflected itself in greater clinical improvement as well as a higher incidence of patients with essentially normal heart sounds postoperatively. In all re-operations for mitral stenosis, the open technique is used.

As in mitral regurgitation, about 15 per cent of the valves are so severely destroyed that without valve replacement only partial benefit can be obtained. This policy has lowered the operative mortality for the closed commissurotomy close to one per cent, as a result of shifting the bad risk patient to the open technique group. The operative mortality in this group is 18 per cent, but one must remember that these patients might be referred to as the salvage group that would not have been benefitted previously. The closed and the direct vision techniques employing a pump oxygenator should not be considered as competing but as supplementary techniques, each of which is to be used where indicated for optimum results in the surgical correction of mitral stenosis.◀

Early Spine Fusion

Results in 35 spine fusions and in the 46 injuries treated conservatively indicate that fusion gives less residual deformity and a lower rate of occurrence. A new interpretation of x-ray findings in a large group of fracture dislocations with slight anterior displacement showed that 50% of them were caused by hyperextension, rather than flexion, as previously thought.

Forsyth, H. F., et al., *J. Bone & Joint Surg.* 41A:17-36,1959.

original article

Prevention of Therapeutically Induced Weight Gains in Hypertensive Patients

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►*Obesity is one of the complications that sometimes arise from an otherwise successful treatment of hypertension with rauwolfia derivatives. In this study 41 patients under care for hypertension were placed on a restricted diet and given an anorectic. Weight losses varied from 6 to 34 pounds in up to 44 weeks.*◄

The widespread use of rauwolfia preparations to reduce blood pressure and maintain normotension has caused excessive weight gains in many hypertensives.[1-6] Indeed, rauwolfia derivatives have been used with some degree of success as appetite stimulants in children and non-hypertensive adults. However, some hypertensives have an inherent predisposition for obesity and a stimulus which leads to excessive weight gains can destroy beneficial effects obtained from reduction of blood pressure. Conversely, weight reduction through dietary restriction, in the hypertensive undergoing medical management, is frequently accompanied by lowering of blood pressure and amelioration of hypertensive symptoms.[7-8] Also, a low-salt diet providing adequate amounts of proteins, minerals, and vitamins helps in control of hypertensive disease.[9] Clinical experience, prior to the introduction of rauwolfia drugs, has demonstrated that a diet of low-salt and low-

*Department of Medicine and Nutrition Clinic, New York Medical College, Metropolitan Medical Center.

1. Wilkins, R. W., & Judson, W. E., *New England J. Med.*, 248:48,1953.
2. Wilkins, R. W., *Am. J. Med.*, 17:703,1954.
3. Freis, E. D., *Med. Clin. North America*, 38:363,1954.
4. Hughes, W., et al., *Am. J.M. Sc.*, 228:21, 1954.
5. Livesay, R. R., et al., *J.A.M.A.*, 155:1027, 1954.
6. Hollister, L. E., *New England J. Med.*, 257: 170,1957.
7. Dinkin, L. G., *New York State J. Med.*, 58:505,1958.
8. Symposium on Nutrition and Disease, Case No. 41, *Postgrad. Med.*, 17:77,1955.
9. Dahl, L. K., et al., *New England J. Med.*, 258:24,1958.

calorie foods succeeds in varying degrees in lowering blood pressure and retarding vascular degeneration. A review of the records of 6 of the patients in this study, previously on low-salt and low-calorie intake alone, reveals that strict adherence to the prescribed diet eventually resulted in a gradual reduction of blood pressure levels. The chief difficulty in this type of treatment is with unwillingness of patients to follow such a regimen. The response is usually too slow, and the patient fails to cooperate fully when an antihypertensive drug is withheld.

Unchecked eating practices lead to obesity and intensified vascular degeneration. Excessive body weight contributes directly to:

1. Greater peripheral vascular resistance and intravascular tension.[10]

2. Cardiac overload, due to intrinsic as well as extrinsic fat deposits, and greater total body weight.[10]

3. Fatty infiltration of tissues causing general impairment of metabolic efficiency.[10]

Since obesity is sometimes a cogenitor of vascular degeneration, every effort must be made to prevent excessive eating by the hypertensive patient, particularly during rauwolfia therapy. At this time, slight weight gain from appetite stimulation may offset whatever beneficial effects might have been derived from the symptomatic relief. Consensus is unequivocal regarding treatment of these patients. Few will follow a rigid schedule of dietary restriction. Every physician recognizes the need for a means of helping to curtail caloric intake. It is imperative that during the initial stages of treatment, the patient learns to practice better eating habits if he is long to survive. The commonly known appetite-suppressants are not suitable for most hypertensives, because these drugs overstimulate the higher centers and adversely affect blood pressure.

Recent experience with a new anorectic, which does not have the usual analeptic properties, suggested clinical trials in a group of hypertensives seen in private practice.[11] Unlike the usual anorectics, this new drug, levo-1-phenyl-2-aminopropane alginate,* is remarkably well-tolerated by patients known to be sensitive to the usual excitatory drugs. The drug may be taken late in the evening to curb nighttime eating, and it has not been reported to disturb normal sleep patterns.

10. Dublin, L. I., *Am. J. Pub. Health*, 43:993, 1953.

*Levonor, Nordmark Laboratories, Irvington, N. J.

11. Gadek, R. J., *J.A.M.A.*, 167:433,1958.

Plan of Study

This study was undertaken to determine the effectiveness of the drug in terms of preventing unwanted weight gains during rauwolfia therapy, and achieving therapeutic weight reductions in patients already overweight. The clinical group comprised 41 private patients undergoing therapy for hypertension. All were receiving or had received, during the past 10 months, some form of rauwolfia. Each was placed on a low-salt, low-calorie regimen and instructed to restrict food intake. The new anorectic was given to help control the appetite and establish a therapeutic regimen.

Some Particulars about the Patients

On the basis of individual medical history these patients were classified in two groups: in Group I those generally amenable to medical direction, in Group II those less cooperative in following medical direction. Members of the latter group were 5 years older, and their hypertensive disease more firmly established. Less favorable results of treatment were expected from this group. One or more of those in Group II suffered concomitantly from at least one of the following: infectious hepatitis, acne, edema, duodenal ulcer, menopausal syndrome, and generalized osteoarthritis. Chronic cholecystitis was found in two women: one, 28 years old and weighing 203 pounds, the other 46 years old and weighing 152 pounds. One man of 37 weighing 252 pounds, had proctitis and elevated blood sugar. Several others exhibited marked anxiety arising from domestic tensions. The 10 women and 1 man in Group II ranged in age from 34 to 68 years (average 50). At the start of the study, 6 weighed 200 pounds or more, 3 were 214 pounds and the lightweight in the group weighed 168 pounds. Pretreatment average of patient weight was 179 pounds. Group I comprised 16 women and 14 men, ranging in age from 28 to 58 years (average 43). At pretreatment examination, 16 weighed more than 200 pounds, 5 in excess of 240 pounds and 1 tipped the scales at 290 pounds. The average pretreatment weight for the group was 204.5 pounds.

Method of Treatment

All patients were instructed about the urgency of dietary restriction, and each consented to a 1200-calorie diet. Sixteen patients in Group I received one 5 mg. tablet three times daily; 12 received the same dosage plus a 5 mg. tablet at 8 p.m.; two received heavier dosage. One of the 16 received 5 mg. at 10 a.m., and 8 p.m. Treatment was carried

out for periods of 5 to 30 weeks.

In Group II, eight patients received one 5 mg. tablet three times daily. One patient received the drug only at 3 and 8 p.m. Treatment was carried out for from 6 to 44 weeks.

Results

Every patient in Group I lost weight in the course of this study, with individual losses ranging from 5.5 to as much as 34 pounds. Weight reductions were two pounds and more per week for seven patients, between one and two pounds per week for 15, and less than one pound per week for eight patients. The average weight loss during this study was 16 pounds.

The degree of patient cooperation determines the outcome in most cases. A man of 37, weighing 274 pounds, lost 34 pounds in 6 weeks, 5.6 pounds per week. A woman of 36, weighing 185 pounds, lost 21 pounds in the same period (3.5 pounds weekly). An uncooperative woman of 36, weighing 170 pounds, who did not follow the prescribed medication or diet, lost only two pounds during 12 weeks. A woman of 53, weighing 214 pounds, and upset by family quarrels, did not cooperate as to medication and diet, and lost only five pounds during six weeks of treatment.

Ten patients in Group II lost weight, while one gained 7.5 pounds. The average loss w 0.33 pounds per week. O woman of 34, weighing 18 pounds at the start reached 1 before being judged as uncoope ative, and in need of an analept drug. Of a group of five, one w careless about taking medicatio another not always cooperativ a third uncooperative during t first part of the 30 weeks she w under treatment.

A woman of 68, weighing 2 pounds, given steroid therapy f rheumatoid arthritis in additio to a no-salt, low-calorie diet, r ceived the usual dosage of t anorectic, 5 mg. t.i.d., for weig control. Despite the weight ga which might be expected fro steroid-induced water retentio this patient lost 11 pounds in 3 weeks.

One man served as a control. man of 44, weighing 214 pound was given a placebo during a pe riod of four weeks and gaine 1.5 pounds, an average of 0. pounds per week. When the sam patient was given 5 mg. of t anorectic three times daily, dur ing a succeeding period of fou weeks, he lost 7.2 pounds, an av erage of 1.8 pounds weekly.

Side Effects

Throughout this study, no sid effects were observed, in spite o the high dosage administered t patients in both clinical groups

The absence of the usual untoward effects of appetite suppressants is noteworthy. The rauwolfia therapy successfully stabilized the hypertension while the anorectic depressed the appetite and safely prevented weight gain.

Valuable, Probably Unique, Action

The new drug, levo-1-phenyl-2-aminopropane alginate was found to exert little or no CNS stimulating action. None of these 41 patients suffered from insomnia, although late evening (8 p.m.) doses were administered. Patients were neither nervous nor euphoric.

There were only two instances of side effects. One patient taking cryptenamine for hypertension, and showing a fair response, required a CNS stimulant. Another patient, with ankle edema, controlled by cryptenamine and a carbonic anhydrase inhibitor, complained of slight nausea. These effects may have been the result of any one or a combination of the medications.

Comments

Forty-one overweight hypertensive patients, ranging in age from 28 to 68 years, were placed on some form of rauwolfia for blood presure reduction as required, and a low-salt, low-calorie diet. Adjunctively, levo-1-phenyl-2-aminopropane alginate was employed to control the urge to eat usually resulting from rauwolfia medication. The drug was administered t.i.d., before meals, in doses of 1 tablet (5 mg.) and, in a number of cases, also at 8 p.m. In a few patients, two tablets three times daily may be required to get the best results.

Observations during this study indicate that this appetite suppressant can safely be used in hypertensives without CNS disturbance and it can be successfully used to combat the nighttime eating habit without causing insomnia. It also accomplished weight reduction in 40 of the 41 cases under study in spite of rauwolfia therapy which ordinarily tends to promote weight gain.

These findings confirm those of an earlier evaluation.[11] In a previous series of 80 patients treated with the anorectic for excessive weight gain, it was adjudged to be as effective as other appetite suppressants, less stimulating, and better tolerated. Because it can be given during the day and the evening, greater freedom in individualizing dosage according to patient needs is allowed. This study appears to extend the usefulness of the drug to weight control in hypertensives, where excess weight is likely to hasten the onset of serious complications. Given in conjunction with proper dietary measures, the drug satisfactorily controls the weight gain

induced by the widely used rauwolfia preparations.

In diabetics, hypertension is commonly preceded and accompanied by obesity, and the introduction of hypoglycemic agents has resulted in the important observation that unwanted weight gain is a side effect, especially with tolbutamide. An anorectic that does not add to the burden already on the cardiovascular system, is an important addition to the agents needed to prevent or control weight gains in the diabetic.◀

Double Aortic Arch: Surgical Correction

Double aortic arch resulting in a vascular ring with various degrees of tracheal and esophageal obstruction and producing ominous clinical symptoms may be amenable to surgical division of the posterior arch. With this procedure the prognosis for children with the anomaly is one of prolonged survival and even cure.

A boy of 2 with a history of dysphagia precipitated by the ingestion of food exhibited wheezing and stridor, especially after eating. He seemed to get worse after 18 months of age. From clinical findings and x-ray studies the impression was gained that an obstructing vascular ring appeared to cause the child's distress, and surgical intervention was recommended. The thorax was entered on the left side through a postlateral incision at the fourth interspace. After the thymus and phrenic nerve were dissected anteriorly to expose the aortic arch, the vagus nerve was dissected posteriorly to expose and retract the recurrent laryngeal nerve. The left subclavian and left and right common carotid arteries were normal, but the right subclavian artery came off a posterior aortic arch. This was temporarily occluded with no change in the child's condition or pulse and the decision was made to divide the vessel to effect an essentially normal aortic arch system. The postoperative course was uneventful. Dysphagia was not noted, and the child's breathing was far less noisy.

An obstructing vascular ring should be suspected in any child showing dysphagia, chronic cough and recurrent pulmonary infections. Noisy respirations and holding the head in hyperextension are corroborative. Diagnosis is supported by x-ray findings of some impingement on the lumens of the trachea and esophagus at the level of the aortic arch. Symptoms due to pressure from a vascular ring may not appear until adult life.

Bernatz, P. E., et al., *Proc. Staff Meet. Mayo Clin.*, 34:173-176,1959.

Eight-year History of a Juvenile Asthmatic

OWEN F. YAW, M.D., *Logan, Ohio*

▶*A preparation containing free theophylline was administered to a girl of 8 presenting a life-long history of asthma and generalized eczema, both resistant to standard allergic and symptomatic management. With this preparation the asthmatic attacks were controlled at onset and the eczema improved.*◀

Many a child with bronchial asthma has a history of eczema in infancy. The fact suggests referral of infants with eczema to the allergist.

Sometimes the general practitioner has the problem of treating the child who has got on poorly on the allergist's regimen—a problem difficult in itself, and an acute problem when bronchial asthma develops despite the endeavors of the allergist.

The proper management of such cases may tax the character as well as the therapeutic resources of the family physician. With corticosteroid therapy, brilliant therapeutic results may be shown to the anxious parents. This knowledge presents a temptation to initiate corticoid therapy before other therapeutic resources are exhausted.[1] Such was the situation in the case to be presented.

Despite treatment by two competent allergists, an infantile eczema persisted and bronchial asthma developed at four years of age. During the next three years the asthma became increasingly difficult to manage. Because of the indifferent results obtained with oral aminophylline and aminophylline combined with a sympathomimetic, an oral theophylline preparation* was given a trial. It has been reported that the unsatisfactory results often observed with oral theophylline preparations could be attributed to slow and erratic absorption of the drug, and failure to reach therapeutic blood levels.[2-4] This preparation is a solution of free

*Elixophyllin®, Sherman Laboratories, Detroit, Michigan.

1. Segal, M. S., *J.A.M.A.*, 169:1070,1959.
2. Waxler, S. H., & Shack, J. A., *J.A.M.A.*, 143:736,1950.
3. Schluger, J., et al., *Am. J.M. Sc.*, 233:296, 1957.
4. Truitt, E. B., et al., *J. Pharmacol. & Exper. Therap.*, 100:309,1950.

theophylline which is rapidly absorbed and in 15 minutes produces mean blood-levels equaling those obtained with IV aminophylline.[3]

After three years of poor response to a variety of therapeutic agents and a progressively worsening condition, the results obtained with this preparation were gratifying.

Case Report

A baby girl of 3 weeks was first seen because of an eczema-like rash on the face. This was treated with mild tar ointments with little success. The child was seen frequently during a period of 2 years because of spreading of her eczema to hands, legs and torso. She was referred to an allergist, who found her to be sensitive to dust, molds and several saprophytic bacteria. A combined vaccine was made and subcutaneous injections of this material were given over the following 6 months. There was little or no improvement in the eczema.

At this time, the parents had an allergist in another city take the child under his care. Of the type of treatment there, nothing is known beyond the fact that some type of subcutaneous injections was given. The child was not seen again by her original doctor for 18 months.

The child was brought to my office in a moderately severe attack of bronchial asthma, her first seizure. She was treated with syrup of Benedryl with moderate relief and the attack was terminated in about 12 hours. The eczema had not changed. For the following year she was seen frequently in attacks of bronchial asthma of varying degrees of severity. She was treated variously with Benedryl, Pyribenzamine, adrenalin, aminophylline and ephedrine compounds—each with varying degrees of success.

Three-and-a-half years later the patient was seen in a truly frightening asthmatic attack. She was admitted to the hospital where vigorous oxygen and adrenalin therapy was instituted. In 36 hours, considerably improved, she was discharged home.

The patient continued to have episodes of asthma. Three months after the initial severe attack, she was placed on oral theophylline. The parents were instructed to give two tablespoonfuls of the preparation (theophylline content 160 mg.) at the first sign of an oncoming asthmatic attack. Close follow-up was kept on the child and in no instance has an asthmatic attack failed to be aborted.

Her parents are unusually intelligent, and they were instructed to experiment with the medication to find out the smallest maintenance dose, as well as the smallest therapeutic dose in an acute attack. A maintenance dose has now been found to be unnecessary and a therapeutic dose in an attack of asthma is as low as one or two teaspoonfuls. Under this regimen the patient has been kept free of any asthmatic seizures by the administration of a therapeutic dose at the onset of any wheezing, and strangely, the eczema has improved markedly.

Unfortunately, in the management of bronchial asthma, the physician initiating steroid the

apy may find himself holding a iger s tail, because of the prob- lems attendant to withdrawal ther py. This applies to the new- est orticosteroids, regardless of their lessened immediate side- effec s.[1]

The knowledge that no harm will come to the patient in later year because of the therapy em- ployed adds to the satisfaction ob- tained in this difficult case. As in previous reports[5] the need for medication diminished as control was gained with oral theophylline and a concomitant eczema of life- time duration greatly improved as the asthmatic condition was better controlled.◀

5. Kessler, F., *Connecticut M.J.*, 31:205,1957.

Chronic Simple Glaucoma: Diagnosis in General Practice

Important diagnostic signs and symptoms include positive family history, required frequent changes in spectacles, headache, periodic dimness of vision, haloes seen about lights, shallowness of the anterior chamber, dilatation of the pupil, and cupping of the optic nerve when viewed with the oph- thalmoscope. If attributable to chronic simple glaucoma, all of these signs and symptoms are caused by increased ocular pres- sure, an instrument for measuring which (the Ocular Hypertension Indicator) is operated on the same principle as the tonometer but is less expensive, easily sterilized and will withstand rough han- dling. The tension is most easily recorded by having the patient lie flat on a table, although a reclin- ing chair will suffice. About one minute should be allowed after instillation of the anesthetic (Dor- sacaine 0.4% or Pontocaine 0.5%) before attempting to touch the cornea. After the footplate of the indicator has been sterilized with alcohol, it is brought to rest di- rectly on the center of the cornea while holding the instrument be- tween the thumb and forefinger. Care should be taken not to slide the footplate of the indicator across the cornea in a lateral di- rection since this may produce a corneal abrasion. The indicator is read from above, during which process the patient fixes his atten- tion on a spot on the ceiling or on his own finger held directly above his eyes. Several readings are re- quired, on different days and pre- ferably in the early morning when the ocular tension is most apt to be elevated, before the diagnosis of glaucoma can be precluded.

Finegan, J. F., *J. Omaha Mid-West Clin. Soc.*, 20:113-114,1959.

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The Painful Heel

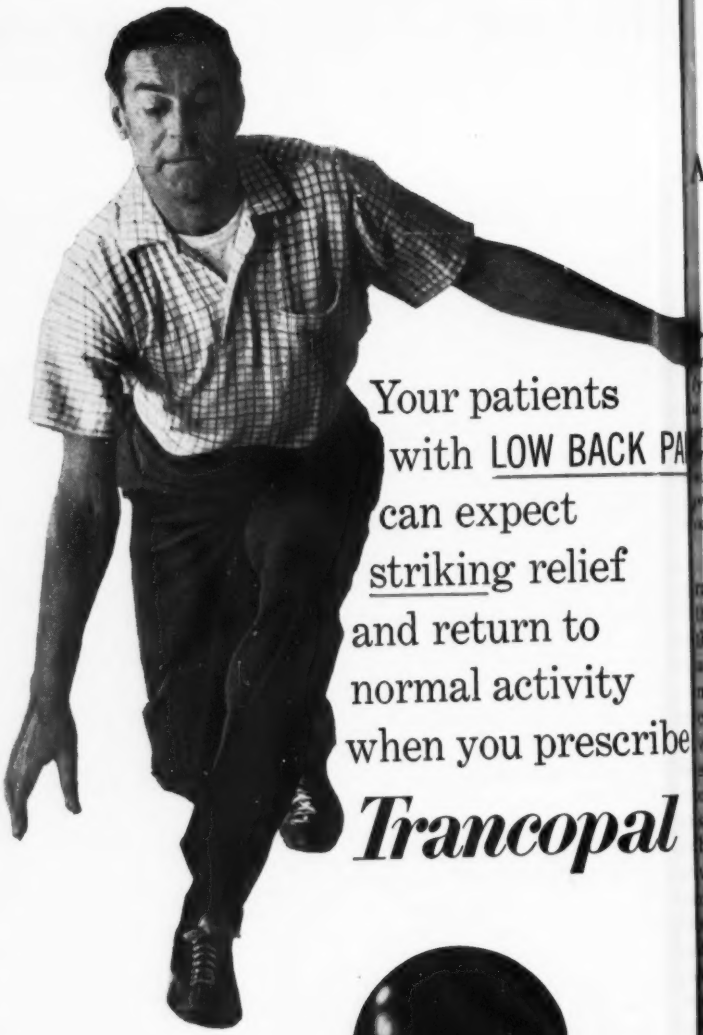
LEONARD MARMOR, M.D.,* *Los Angeles, California*

Plantar facitis is the actual cause of this heel pain, and not the "bone spur" seen in the region of the os calcis. Neither conservative methods nor surgery are indicated in these cases because patients respond very well to a therapeutic combination of hydrocortone acetate and xylocaine.

The problem of the patient with a painful heel has confronted most physicians in the course of their practice, and resort to many conservative methods often fails. The use of arch supports, heel pads, contrast soaks, ace bandage, and even crutches is well known to all. The patient continues to have pain in his heel on weight bearing. X-rays of the foot may or may not show a so-called "bone spur" from the under side of the os calcis in the region of the origin of the plantar fascia. Many patients have been operated upon for this condition with relief of their symptoms.

An attempt was made to relieve these symptoms by the use of hydrocortone acetate injections. Patients coming into the clinic with complaints of pain in the region of the heel were examined and the foot x-rayed. Many of them showed what would be called a bone spur, and palpation revealed a point of tenderness along the medial side of the foot just distal to the heel pad. Two cc. of 1% Xylocaine and 1 cc. of (25 mg.) hydrocortone were injected into the region of the plantar fascia origin. Patients noted almost immediate relief from the Xylocaine with a return of symptoms in 8 to 10 hours. However, at the end of a week to two weeks at the longest, symptoms were completely relieved. This procedure has been applied to the patients seen in our clinic with marked relief of their symptoms.

From the Department of Surgery, Division of Orthopedic Surgery, University of California Medical Center.



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case report

Aortic Dissection (Dissecting Aneurysm)

DALE GROOM, M.D., E. F. PARKER, M.D., and
WILSON GREENE, M.D.,* *Charleston, South Carolina*

Current developments in cardiac surgery have made what was formerly a post-mortem academic discussion a correctable possibility. Operational possibilities of this emergency are presented with a record of a patient whose post-operative course improved satisfactorily without significant complications.

One of the most dramatic and rapidly fatal vascular accidents is that of spontaneous dissection of the aorta. Customarily referred to as dissecting aneurysm, it might more properly be designated according to its basic pathology which is that of a splitting and dissection between layers of the wall of the aorta by blood under pressure, rather than a dilatation or bulging of a localized area of the vessel wall. Until recently the clinical diagnosis of this lesion, which has been recognized pathologically for many years, was of more or less academic interest inasmuch as there was no available treatment capable of altering the course of the disease and preventing the ultimate rupture and sudden death. The advent of surgical procedures for repair of aortic dissection has brought with it a new and more fruitful interest in the ante mortem diagnosis of this disease.

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Clinical and Pathologic Aspects

Predominant in the clinical picture of aortic dissection is pain. Characteristically it is sudden in onset, of extreme severity, often "tearing" in nature and progressing in stages from above downward. Location of the pain is dependent upon the site of the lesion; with involvement of the arch it is typically substernal with radiation through to the back, notoriously simulating that of myocardial infarction. Blood pressure may rise with the unremitting pain, or may fall to shock levels as blood fills and distends the adventitious lumen of the aorta. Often accompanying extension of the dissection are manifestations of partial or complete occlusion at

the origins of the various branches of the aorta, including differential blood pressure changes in the extremities, renal impairment, or paraplegia resulting from involvement of the intercostal branches supplying the spinal cord. Similarly a coronary artery may be occluded at its ostium or the aortic valve may be rendered incompetent, signifying dissection in the proximal portion of the aorta. Rupture of the thin-walled false lumen with fatal hemorrhage into one of the body cavities is the rule within hours, days or weeks, although rarely the dissection may remain intact for months or even years without gross impairment of arterial blood supply. In such cases the double-lumen area of aorta may be a surprise finding at autopsy of a patient who has had perhaps evanescent neurologic signs following what was construed as a heart attack.

Traditionally this disease has been ascribed to a medial degeneration of the vessel allowing dissection by blood under pressure following a tear through the intima. Its association with hypertension, with Marfan's syndrome, and perhaps with pregnancy and coarctation has been noted. Although it is predominantly a disease of middle age and beyond, rarely, it seems, does the tear occur at the base or edge of an atheromatous plaque. Notable s t fact that the aorta, which can demonstrated to be capable withstanding many times the h draulic pressures encountered the human body, can be split markably easily between its la ers when they are separat longitudinally. This, together wi the observed occurrence of aor dissection without an obvious timal tear, has led to the more cent theory that the initial lesi may be hemorrhage from the va vasorum within the wall of t vessel, contributed to by oth vessels (including branches the aorta) as the dissection pr ceeds, with the rent in the intim being the consequence rath than the instigating factor in t process. A consideration of the mechanisms is of practical impo tance in the surgical approach aortic dissection.

Surgical Aspects

Location and extent of the ar of dissection, whether this be r lated to the location of the init lesion or not, is of course cruc to the surgical approach as well to the clinical manifestations a prognosis. About 90% of a seri of 22 cases from the Mayo Cli had some involvement of the ac tic arch, with the descending tho acic and abdominal portions the aorta involved in almost many instances. Usually the in

mal tear is found in the ascending portion, just above the semilunar valve, or in the region of the ligamentum arteriosum and left subclavian artery. A less common site is in the abdominal aorta. No consistent relationship has been demonstrated between size of this tear (which is sometimes transverse sometimes longitudinal, and commonly on the order of 1 cm. or so in length) and extent of the dissection.

The 1935 report of a case of dissecting aneurysm operated upon by Gurin, Bolmer and Derby has brought them credit for the first attempt at surgical intervention. Almost twenty years then passed before this lesion was generally regarded as potentially amenable to operation. The advent of mechanical pump oxygenators for extracorporeal maintenance of circulation has opened the way for more definitive repair of the lesion under direct vision. At first the objective was that of closing the tear in the intima with the idea of thereby isolating the false lumen from the systemic blood pressure, halting the progress of dissection, and averting rupture of the adventitia and fatal hemorrhage. Such a procedure has certain obvious limitations and does not allow for any other source of dissecting pressure, either primary or secondary. A second method of attack was one of fenestrating the intima, creating a second communication between the normal and the false aortic lumen, presumably for re-entry of the blood from the dissected area back into the normal aortic lumen. It is questionable whether this would materially alter the pressure gradients or decrease the likelihood of rupture, the major cause of death. Furthermore, the fenestration approach does not take into account the observation that many of these cases already have two tears in the intima. From a practical standpoint it would appear that any section of aorta having a dissection of its wall should either be repaired by apposition of the dissected layers, obliterating the false lumen, or should be replaced by a mechanically competent structure, i.e., a graft. DeBakey has reported more than a score of cases (in which the dissection was primarily in the descending thoracic aorta) so treated with an operative mortality of between 25 and 30%.

Case Report

A 59 year old power-line foreman was brought to the Medical College Hospital by ambulance with the diagnosis of dissecting aneurysm. With him were two chest roentgenograms substantiating that diagnosis, one made on a routine examination a month previously, the other dated the day prior to admission. He was known to have had asthma and pulmonary emphysema for many years with symptoms of a decreased respiratory reserve, and for several months had

received cortisone daily for control of his asthma. Also of interest was the history of a long standing hypertension, group II, for which he had been treated with apresoline.

Two days previously, while sitting quietly at home watching television, he had experienced a sudden onset of severe pain in the epigastrium radiating through to the back. He was immediately unable to stand and noted paresthesias in his legs and feet. On examination his blood pressure was found to have fallen from its usual average of 180/110 mm. Hg. to near shock levels. Next day the pain continued, but with an ascending distribution extending up into the midchest, and he became mentally confused, disoriented, and required restraint. Urine output nevertheless remained adequate. His blood pressure then gradually rose to its former hypertensive range and motor function returned to his lower extremities.

The significant findings on admission were those of acute delirium, hypertension, and advanced pulmonary emphysema with distant respiratory and heart sounds and a dusky hue to the lips and nailbeds. Arterial pulses were unimpaired in all four extremities although aortic pulsation could not be felt in the abdomen. There were no objective neurological abnormalities. Laboratory studies including the complete blood count, urinalysis, hematocrit and blood urea nitrogen were within the normal ranges. An electrocardiogram was not remarkable except for a sinus tachycardia.

Roentgenographic examinations of the patient's chest and abdomen disclosed aneurysmal dilatation of the entire descending thoracic aorta, extending into the arch, and a generalized pulmonary emphysema. Aortograms were then made by means of a catheter inserted through the left brachial artery as far as the mid-portion of the ascending aorta. Radiopaque dye injected through the catheter was observed to produce opacity in only about two-thirds of the width of the dilated arch with none of the dye passing into the surrounding false lumen of the vessel.

For two days thereafter the patient continued to have pain which subsequently extended into the lower back. His temperature rose to 101 - 102° F. and he became exceedingly restless in spite of analgesics, sedation, and supportive therapy. Nevertheless his blood pressure became stabilized at about 160/90, his electrocardiogram remained unchanged, and no cardiac murmurs were audible at any time nor was there any other indication of further spread of the dissection proximally.

In view of the obvious prognosis and the urgency of the patient's situation, operative intervention was decided upon with the intent of finding and suturing, if possible, the tear in the intima and possibly obliterating at least a portion of the dissecting lumen—this despite the admittedly high risk and the known involvement of the arch. Accordingly the patient digitalized and given replacement cortisone therapy, and a left thoracotomy was performed on the fourth hospital day, the sixth day after onset of his acute illness.

The aorta was observed to be diffusely enlarged to approximately 8 cm. in diameter from the diaphragm to the origin of the innominate artery. Proximal to this point there was no evident abnormality and all major branches of the arch could be seen to pulsate normally. A mechanical pump apparatus was then employed to bypass blood from the left atrium into the femoral artery at a flow rate of 1200 to 1400 ml. per minute. The aorta was mobilized for a distance of 12 cm. distal to the subclavian artery (necessitating division of six intercostal arteries on the left, leaving the corresponding branches on the right intact) and the dissected area of aorta was isolated proximally and distally with occluding clamps. Between these clamps the vessel was then opened longitudinally and an inner lumen of normal size was found, encompassed by an outer lumen formed by the dis-

sected layers of wall and filled with blood and clots. Rupture through the remarkably thin outer layer appeared to be imminent.

After what seemed at first a fruitless search, a laceration about 1 cm. in length was found in the intima of the aorta adjacent to the point of attachment of the ligamentum arteriosum. Because of the precarious structure of the adventitial wall, the possibility of an additional undisclosed rent in the intima, and the feasibility of accomplishing a more definitive repair in the dry field provided by the by-pass pump, it was then decided to resect as much of the dissected area as practicable and replace it with a graft. A 9-cm. length of aorta extending from the origin of the left subclavian artery distally and including the area of intimal rupture was removed. Continuous annular sutures between the intima and adventitia were employed to obliterate as much of the remaining false lumen at both ends as possible after removal of enough clot to allow apposition of the dissected layers. Continuity of the aorta was then restored by insertion of a Teflon graft by end-to-end anastomoses. Total time on the by-pass pump was one hour and forty minutes, during which the patient received a total of 4500 ml. of whole blood. Except for a transient cardiac arrhythmia and marked restlessness and confusion his postoperative course was one of gradual mental and physical improvement. He was discharged from the hospital as an ambulatory patient three weeks after admission. Follow-up examinations of this patient one, three, and twelve months after operation revealed no recurrence of aortic dissection.◀

J. South Carolina M.A., 55:246-248,1959.

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Acute Bacterial Endocarditis Due to Micrococcus Pyogenes

E. W. SANDERSON, M.D., *Sioux Falls, South Dakota*

►*A case of acute bacterial endocarditis due to micrococcus pyogenes var. aureus superimposed upon congenital heart disease in a girl of 14 is presented with a brief discussion of the symptoms, pathology and therapy of that disease. Duration of therapy is as important as the selection of agents.*◄

Acute bacterial endocarditis is defined by Friedberg as an inflammatory disease of the endocardium usually caused by pyogenic organisms and characterized by a systemic infection with embolic or metastatic phenomena and if untreated terminates fatally within six weeks. It is distinguished from subacute endocarditis by a shorter duration, usually by a different causative organisms, and by differences in clinical and pathological features. These differences may be uncertain and both diseases may overlap with regard to all of the usual distinguishing features. As in subacute endocarditis, the fundamental mechanism of acute bacterial endocarditis consists of bacterial invasion of the blood stream with localization of the bacteria on the endocardium, which is often the site of a previous abnormality, and persistent batermia, toxemia and embolization due to the bacterial vegetations on the endocardium.

The acute disease is due, most commonly to hemolytic streptococcus, pneumococci or staphlococcus aureus. Other organisms responsible for acute bacterial endocarditis may be N. gonorrhoeae, N. meningitidis, E. coli, Pseudomonas, Klebsiella, Actinomyces bovis, Micrococcus rugatus, spirilla, and B. anthracis. The most common predisposing factor is previous valvular or congenital heart disease which is present in about seventy per cent of the cases. Because of the greater virulence of the causative organisms in this group, their transient in-

vasion of blood stream is more apt to result in a bacterial focus on normal valves than in a transient bacteremia with less virulent organisms causing subacute endocarditis.

In contrast with the subacute cases, acute bacterial endocarditis is almost always preceded by some overt local or general infection due to one of the above mentioned organisms. The original infection may be active or apparently healed by the time the bacterial endocarditis is manifest. Sometimes bacterial invasion of the blood stream follows operative procedure in an infected organ or tissue; however, in a considerable number of cases, the infection arises from some undetermined focus or may be a terminal infection in the course of a chronic or fatal disease such as portal cirrhosis, leukemia or agranulocytosis. Age, sex and race do not appear to be significant factors.

Pathology

The pathology, as in the subacute cases, are vegetations usually superimposed on thickened, scarred vascularized rheumatic valves or on congenital cardiac lesions. The left side of the heart is chiefly involved. Vegetations of the right side of the heart are caused most often by the gonococcus but even this organism is more likely to attack the mitral or aortic valves. Also, ulceration is a feature of the acute cases and because of this process, aneurysms and perforation of the valves and loss of substance are more common than in the subacute cases. Vegetations are found on the mural endocardium much more rarely than in subacute bacterial endocarditis. The left auricle is uncommonly affected but occasionally, there are vegetations on the chorda tendineae and papillary muscles of the left ventricle. The intraventricular septum and rarely the heart wall may be perforated.

Microscopically, the vegetations are composed of solid bacterial masses of fibrinous material through which bacteria are profusely scattered through the very surface of the lesion. Blood platelets are infrequent and there are numerous polymorphonuclear leukocytes and the subjacent valvular tissues shows extreme necrosis and separation. The bacteria extend into the collagenous structure of the valve. Healing is absent or minimal. There may be numerous focal lesions consisting either of myocardial submiliary or microscopic abscesses or infiltrations of round cells and polymorphonuclear leukocytes. Abscess formation occurs particularly in staphylococcic or gonococcal infections. Pericarditis is more common in the subacute form. In twenty to forty per cent, there is a purulent or sanguino-

purulent pericarditis which may be discovered at post-mortem. Pathological alterations in other organs such as the spleen and kidneys vary considerably in frequency, severity and kind, according to the nature of the causative organism and the duration of the illness.

Diagnosis

The clinical picture is that of a general infection or septicemia and differs in no way from that in septicemias without bacterial endocarditis; therefore, the symptoms of acute bacterial endocarditis are those of a general toxic nature with embolic and vascular and cardiac symptoms. The onset is apt to be abrupt with fever and perhaps a chill. Sometimes the onset is indicated by persistent or recurrent fever when the initial infection has finally healed. Profuse diaphoresis, marked weakness and various cerebral and psychic disturbances may occur. Embolic phenomena are less frequent than in subacute bacterial endocarditis, probably because of the short duration of the disease. Infarction, when present, is generally purulent. Cutaneous manifestations are frequent and the petechiae are frequently definitely embolic in nature and may have a white center which may or may not be elevated. Those with elevated centers are really miliary abscesses. Cardiac symptoms consist chiefly of organic murmurs due to previous valvular or congenital disease with changes in the quality, intensity or radiation of murmurs previously present or of the development of mummurs which were previously absent. In Staphylococcus aureus endocarditis, a positive blood culture is usually readily obtained. In the presence of a cardiac murmur, bacterial endocarditis is probable even before embolic manifestations purulent pericarditis, metastatic pneumonia or abscesses, petechiae or splenomegaly are observed.

In a review of the literature from the twelve year period between 1936 and 1948 by Marion Jones, twenty-nine case reports were found of acute or subacute bacterial endocarditis due to micrococcus pyogenes. Eighteen of these cases were in detail. Eleven of these cases were superimposed upon rheumatic heart disease, four congenital heart disease, one with syphilitic heart disease and one with chorea. There were twelve apparent recoveries with three month to four year follow-ups. Alpha-hemolytic streptococcus or streptococcus viridans has been found to account for ninety to ninety-five per cent of all forms of endocarditis. The remaining five to ten per cent are caused by a great variety of other micro-organisms which may be common saprophytic inhabitants

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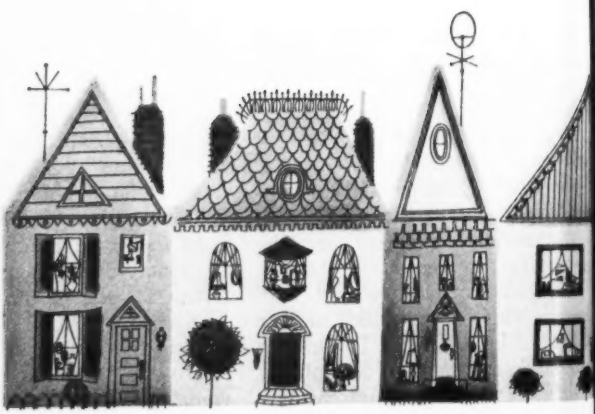

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of the human body, which by chance, invade the blood stream or by micro-organisms usually of greater pathogenicity which are not normal inhabitants but may be introduced from without the body.

Case Report

The patient, a white girl of 14 was admitted to the hospital on July 1, 1957 with the history of having had an upper respiratory infection one month previously with a persistent chronic cough which was non-productive. On the morning of admission, she developed headache, malaise, anorexia, nausea but no vomiting, chills, fever, weakness and numbness of the left arm. Her mother noted cyanosis of the lips, fingers and feet during the day. System review was non-contributory.

Past history revealed that she was born with congenital heart disease and that she was hospitalized elsewhere in 1954 for a diagnostic survey including cardiac catheterization. Blood samples revealed slight arterialization of the blood in the right ventricle. The pulmonary artery pressure averaged 90/40. The left to right shunt was calculated to be about 15 per cent of the left ventricular output. The most unusual finding was a localized constriction of the right pulmonary artery with a fall in pressure to 50/30 beyond the constriction. There was also a patent foramen ovale without evidence of intra-atrial shunt. Their diagnosis was:

1. Intraventricular septal defect.
2. Patent foramen ovale.
3. Localized constriction of the right pulmonary artery.

She had the usual childhood diseases and also infectious hepatitis. She has been cyanotic previously when febrile. Her physical activity had been moderately restricted throughout her lifetime.

Physical examination revealed a well developed and nourished girl who appeared cyanotic in the extremities and acutely ill. The lungs were clear to percussion and auscultation. The heart was not enlarged. There was a sinus tachycardia of 150/minute with a systolic murmur loudest in the right third interspace but heard over the precordium with Gr. II intensity. The liver and spleen were not palpable and no petechiae or edema was noted. Blood pressure was 120/60. Temperature 100.6 and respirations 24.

Laboratory: Urinalysis normal. Sediment included 3 to 5 wbc/hpf and squanous epithelial cells. Hb. 14 gms., RBC 4.8 million, WBC 9,400. Differential: neutrophils-segs 72, bands 15, lymphocytes 11 and monocytes 2. ESR 20 mms/hr. VDRL negative.

Hospital course: During the night following admission, she developed giant urticaria of the arms and legs after receiving Tuinal and ASA. (She has since received both drugs without allergic reaction.) The following day and night she complained of a progressviely severe sore throat, dysphagia and stiff neck. The urticaria cleared quite rapidly with antihistamines. Physical examination revealed slight edema of the throat and some menengismus but no true nuchal rigidity. A spinal tap was performed in the evening. Laboratory exam: Chloride 128 meg/liter. sugar-75 Mg.%. Protein 47.2%. Cell count-2 mononuclear cells and 3 polymorphonuclear cells per Cmm. Colloidal gold-normal curve-11110000. Throat culture-alpha streptococcus, Hemophilus hemolyticus and Neisseria catarralis.

Aqueous Penicillin G. 200.000 U. q. 3 h. was started because of the fever up to 105.6 R., the subjective sore throat and the critical condition of the patient. Twelve hours later the temperature was 99 degrees rectally and she was subjectively and objectively much improved. The aqueous penicillin G was discontinued in favor of procain penicillin G, 1 million U. every twelve hours and she continued to be afebrile throughout the hospital

stay except for a spike to 100.6 on the enth hospital day. Three blood cultures and the spinal fluid culture grew micrococcus pyogenes var. aureus, coagulase positive. These cultures were sensitive to all antimicrobials except the sulfonamides. After the positive cultures and sensitivities were reported. Erythromycin 250 mgs. every six hours was added to the therapeutic regime to give the patient the benefit of combined anti-microbial therapy. Subsequently three random blood cultures with penicillinase added were sterile. The patient remained essentially asymptomatic throughout the rest of her hospital course except for some nausea and heartburn attributed to erythromycin intolerance. The Penicillin was continued for 24 days and a total dosage of 47.8 million units. The erythromycin was continued for two weeks after discharge from the hospital 31 days after admission for a total of 40 days.

Throughout the hospital stay, the heart murmurs were noted to change occasionally from a systolic murmur loudest at the right third interspace to a continuous murmur in the same area. Her weight remained stable during the illness; however, she gained 12 pounds within six weeks after dismissal. The temperature was checked t.i.d. at home for three weeks after discharge and remained normal. Frequent follow-up visits since discharge have not been remarkable. She has been carrying a full schedule in school this year; however, she does not participate in physical education activities.

Discussion

The therapeutic implications of this case are manyfold. There are three primary factors to consider in the selection of treatment in acute or sub-acute bacterial endocarditis:

1. The selection of the drug.
2. The total daily dosage.
3. The length of therapy.

The penicillin in this case had been given several days prior to the report of the positive blood cultures and the patient had made an excellent clinical response. Since penicillin is a bactericidal agent, it was elected to continue this drug parenterally and to add erythromycin for combined antimicrobial therapy. The addition of the erythromycin to be used in conjunction with penicillin may be questioned by some authorities; however, it has been definitely proven in large series of cases that micrococcus pyogenes is resistant to penicillin in sixty to seventy per cent of all strains and that occasionally this organism becomes rapidly resistant to penicillin. Erythromycin has been found to be quite efficient in most infections of staphylococcus and has relatviely few side effects. It is considered by some to be bacteriostatic and by others to be bacteriocidal. Bacteriostatic drugs are not considered to be curative in cases of endocardial vegetations. In retrospect, the clinical response of the patient, probably justifies the selection of drugs in this case in which a definite bactericidal drug and a drug which may be bactericidal or bacteriostatic were used as combined therapy.

Subacute and acute bacterial endocarditis have been treated to

a reasonable degree of success since about 1945. Prior to chemotherapy and antibiotics it was almost universally fatal. In general, about seventy per cent of these cases recover, however, there is a wide mortality rate in individual reports. It is discouraging to note that the mortality rate has not changed appreciably since the use of penicillin became available during the past fifteen years, in spite of the wide range of antimicrobials that are now available. Patients with bacterial endocarditis do not defend themselves against infection as evidenced by the outcome of untreated disease; therefore, successful therapy must accomplish in the host, almost complete eradication of the offending organism without appreciable aid from the host. Any suitable microbial agent must have certain characteristics:

1. It must be bactericidal.

2. Its administration over a long period of time must not be associated with serious side effects.

3. It must penetrate clots.

4. It must obtain a blood level capable of killing the offending organisms.

The tetracycline group, chloramphenicol and the sulfonamides do not fulfill these criteria and must be labeled inferior. Bacitracin, Neomycin Polymyxin B are toxic drugs and must be used with caution and vigilence. Penicillin, and streptomycin alone or in combination, fulfill the necessary requisites in most instances and this combination has been proven by clinical experience. The design of the ideal therapeutic program is to administer a drug in sufficient concentration in the serum and within the vegetations higher than the sensitivity in vitro. These concentrations must be maintained over a sufficient period of time to assure penetration to the base of the avascular vegetations in which area, the organisms are lodged. Penicillin and streptomycin and perhaps other antibiotics have a synergistic action against some organisms. Two to four grams of probenecid (benemid) daily by mouth enhances penicillin blood levels by delaying urinary secretion. Penicillin may be given by various routes including subcutaneous, intramuscular or intravenous drip as well as orally and intramuscularly. Several articles in the recent literature have shown that in spite of a few cases of apparent cures with oral Penicillin V, that this route of administration is not at therapeutically effective as the parenteral route. Therapy should be continued for a minimum of three weeks after subsidence of active infection.◄

South Dakota J. Med. & Pharm., 12:265-268. 1959.

Improvement of Hearing with Surgical Techniques

R. J. McQUISTON, M.D., *Indianapolis, Indiana*

► *Although new mobilization techniques employed in the treatment of deafness due to otosclerosis are effective, due largely to improved lighting and magnifying procedures, fenestration remains the most effective treatment available, being about 88 per cent effective when good auditory nerve function has been retained.*◄

Before any operative procedure can be successful it must be established that the auditory nerve is capable of receiving 500, 1,000 and 2,000 sound vibrations at, or above, the 30 db. level in order to understand the spoken voice. When this is established surgery is directed at mobilizing the perilymphatic fluids of the internal ear to enable them to carry the sound waves to the nerve endings in the cochlea.

To accomplish this, both the round and oval windows must be functioning properly. If either is inhibited by bony fixation or infection, the peri-lymph will remain immobile, thereby preventing the sound waves from stimulating the auditory nerve.

New Mobilization Techniques

Early attempts to mobilize the stapes in deafness due to otosclerosis were not successful. However, re-introduction of this operation in 1953 has been associated with a high degree of success, due largely to improve lighting and magnification techniques. With better magnifying equipment it is now possible to visualize the foot plate itself as well as the otosclerotic lesion fixing the foot plate in the oval window. Direct attacks are now made upon the foot plate with small needles, drills, and chisels, thereby loosening and removing portions of the otosclerotic bone around the foot plate and facilitating its movement without disturbing the crura.

Another approach is the creation of a window directly into the

foot plate of the stapes. To date, however, this method has been successful in only 50 per cent of cases, and still should be regarded as experimental. Reasons for the high percentage of failures include crural fractures and the refixation of the foot plate after it has once become mobilized.

At no time should stapes mobilization be considered a substitute for fenestration, but rather a preliminary procedure which might be successful. If it fails, it can be followed by the fenestration operation at a later date.

Fenestration

Today this procedure gives the patient with deafness due to otosclerosis his best chance of hearing improvement, being about 88 per cent effective when good auditory nerve function has been retained. The trans-tympanic approach is of value in the treatment of hydrops of the labyrinth, or in Mèniére's disease for the relief of vertigo. In recent years these conditions have been approached by trans-tympanic labyrinthotomy, accomplished by elevating the ear drum, exposing the ossicular chain, then severing the incus from the head of the stapes. After the stapes is removed from the oval window, opening the internal ear or labyrinth, a small aspirating tip is placed in the vestibule and the endo-lymphatic membranous labyrinth removed by aspiration. The ear drum is then replaced in its normal position and pledgets of gelfoam packing soaked in topical thrombin placed against it and in the external canal. The operation is completed in about 20 minutes without shock to the patient.

The following operative techniques are considered reconstructive plastic procedures and can be carried out successfully only after bone necrosis and disease of the affected parts are thoroughly controlled by antibiotic therapy or surgery.

Myringoplasty

This technique is employed when a permanent central perforation of the ear drum is encountered without evidence of bone necrosis, granulations, cholesteatoma, or ossicular chain damage. The perforation is closed by removing the outer or epithelial layer of the drum and the adjacent external canal with a curette. A full thickness skin graft is placed over this perforation and held in position for about 10 days with gelfoam pledgets soaked in topical thrombin.

Epitympano-Mastoidectomy

This is employed when the ossicular chain is intact, but a marginal perforation with attic bone necrosis exists in which granulation tissue or attic cholesteatoma may be present. The technique

requires approach by the external auditory canal route and eradication of the diseased and necrotic bone in the mastoid process exposing the attic bone and adjacent portions of the ossicular chain. The integrity of the remaining portion of the ear drum and ossicular chain are preserved. After microscopic removal of granulation tissue and cholesteatoma is completed a full thickness skin graft is applied to the remaining bared surface of the ear drum, the ossicular chain and the adjacent mastoid cavity.

Columella Type Tympanoplasty

This procedure is indicated when the disease process has already caused an interruption in the ossicular chain along with necrosis of the mastoid and attic cells. It requires complete removal of all disease in the mastoid cells and the midlde ear, care being taken to preserve the stapes so that it will not be dislocated in the oval window. To achieve this the lower facial ridge must be radically lowered to permit good apposition of the skin graft used later at the head of the stapes. After this is done the skin graft is placed over the middle ear and mastoid cavities, and at the head of the stapes.

Total Tympanoplasty

This technique is employed when all of the ossicular chain including the stapes has been destroyed. It requires total mastoidectomy and skin graft covering the round window area but leaving an air space communicating with the Eustachian tube. The middle ear is exposed and left open. With this method the skin graft acts as a baffle over the round window area so that sound waves will strike the unprotected oval window wtih more intensity. The method allows a greater possibility of endo-lymphatic fluid mobilization in the internal ear with a greater chance of hearing improvement. In cases where the infectious process has caused a labyrinthine fistula, this may be converted into a functioning fenestra (as employed in the fenestration operation), and then covered with a skin graft.◀

J. Indiana M.A., 1:51-54,1959.

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Obstetrical Factors in the Etiology of Cerebral Palsy

NICHOLSON J. EASTMAN, M.D., *Baltimore, Maryland*

►*Some predisposing factors in cerebral palsy are: carbon monoxide poisoning in the mother, prematurity, neonatal asphyxia, Rh factor incompatibility, and certain vitamin deficiencies. Traumatic labor did not appear to be a factor. Further research may reveal neurochemical phenomena.*◄

Of 13 pregnant women suffering severe carbon monoxide suffocation, both the mother and the fetus died in some cases while in others only the fetus died. The pregnancies in all of eight cases in which the mother and fetus survived continued to term, carbon monoxide intoxication in these cases having occurred at various times from the second month to near term. All eight of these infants showed psychomotor disturbances, such as mental retardation (in some cases idiocy), hypotonia of the neck, hypertonia or spasticity of the extremities, anatomic anomalies, and hydrocephalus. Two of the infants died. Postmortem examination of one, aged six days, revealed hydrocephalus, and of the other, who died at nine days, extensive softening of the basal ganglia. The most common disorder in these infants was spasticity of the extremities, while other psychomotor abnormalities occurred in five of the eight. Intoxication had occurred between the third and eighth months of pregnancy in the five infants with spastic symptoms, and during the eighth month in the one infant with athetosis.

In a series of 628 cases of cerebral palsy surveyed with respect to obstetric etiology, two factors stand out: prematurity (27 per cent incidence) and neonatal asphyxia (23 per cent incidence). A history of prematurity was found in 50 per cent of cases of symmetric spastic diplegia and paraplegia, but in only 14 per cent of cases of spastic hemiplegia. In contrast, neonatal asphyxia was 3½ times more common in this last group than among that of

those with symmetric spastic diplegia. None of these infants was delivered by cesarean section, so that the trauma of labor can not be ruled out as a causative factor.

A review of 478 cases of cerebral palsy showed severe icterus in the neonatal period in 68 per cent of the athetosis, 11 per cent of the hemiplegia, 17 per cent of the paraplegia, and 9 per cent of the tetraplegia cases. A history of severe asphyxia was found more frequently in the cases of athetosis than in those of any plegia. Rh negative mothers with Rh positive infants were noted in 39 per cent of the cases of athetosis investigated, in 14 per cent of the hemiplegia, in 2 per cent of the paraplegia, and in 1 per cent of the tetraplegia cases. It is significant that Rh antibodies were found in a total of 23 cases, 22 of which were of athetosis.

These two studies suggest that any intelligent approach to the etiology of cerebral palsy must be based on the type of the condition with the specific obstetric injury.

As neurochemical research advances, it becomes increasingly evident that a wide range of complex enzymatic aberrations may cause various types of brain injury. Twelve gravid women, all in the first trimester and all presenting urgent indications for therapeutic abortion, were given oral doses of the potent folic acid antagonist 4-amino pteroylglutamic acid over a period of two to five days. In pregnant rodents the severe folic acid deficiency resulting from administration of this substance causes rapid death and absorption of the embryo. Among the 12 women given this preparation immediate death of the fetus occurred in the five earliest pregnancies, followed within 17 days of abortion. In a sixth case abortion occurred within 17 days and death of the embryo near the time of expulsion, this fetus having a meningocele. Spontaneous abortion ensued in four additional cases only after a second course of the drug. In the two cases failing to abort by this method surgical intervention was employed, revealing one hydrocephalic fetus and the other with cleft palate and harelip.

These twelve cases demonstrate the necessity of folic acid to fetal life and normal development. The same is true of vitamin B_{12}. Since both folic acid and vitamin B_{12} are so intimately associated with hematopoiesis, it may be overlooked that this role is an example of their essentiality in the formation of nuclear protein throughout the body. The fact that vitamin C is also much higher in fetal than in normal blood is of particular interest in the present condition since it is known that deficiency of this vitamin alters normal folic acid metabolism. Folic acid also seems to

be involved in progesterone metabolism. The mechanism of action and the interrelationship of vitamin B_{12}, folic acid and progesterone are extremely complex and much remains to be learned about them as factors in the causation and prevention of cerebral palsy.◀

Connecticut Med., 23:316-319,1959.

Recurrent Erosion of the Cornea: Cure and Prophylaxis

Although this disease has apparently developed spontaneously in a few cases it usually follows trauma, and is sometimes known as "finger-nail keratitis" because of its frequency in parents scratched by their infants. Recurrence upon first opening the eyes in the morning is a diagnostic feature. The epithelium is torn loose from Bowman's membrane and hangs as a characteristic filament, the eye red, painful, and acrimeling profusely. In a few hours the epithelium reforms and the eye becomes white and comfortable, only to relapse some time later. Although the mechanism underlying the erosion is not known, peristence of epithelial edema seems to be a factor.

Of 32 cases, all but 2 were posttraumatic. The original corneal injury, extensively damaging to the epithelial surface, had been caused by children's scratches in 8 cases, fragments from broken eyeglasses in 4, and glancing blows with stiff paper or stiff wire in 7. The clinical picture observed in all 32 cases showed the lesion located just below the pupil in the midline (regardless of the site of the original injury), appearing upon opening the eye in the morning. Only 1 case was complicated by infection.

Treatment in the first 20 cases was classical (removal of loose epithelium, cauterization with tincture of iodine, and patching). Cures were effected in 12, while relapses requiring further cauterization occurred in 8. Treatment in the remaining 12 cases consisted of frequent instillation of a steroid suspension or solution during the first 48 hours or until the epithelium was intact, followed by 5% boric ointment nightly until one month after disappearance of the edema. These patients were also cautioned to open their eyes slowly and gently. Under this regimen there have been no relapses to date. This same combination has been used prophylactically in 11 patients with corneal injuries of the type expected to lead to recurrent erosion, so far without recurrence of the disease.

Thygeson, P., *Am. J. Ophth.*, 47:48-52,1959.

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EATON LABORATORIES, NORWICH, NEW YORK

Treatment of Peptic Ulcer with Chymotrypsin

A. A. MOZAN, M.D., *Chicago, Illinois*

►*A pancreatic enzyme was administered intramuscularly either alone or in conjunction with other agents in treating 78 patients with gastric ulcer. Among the 90 per cent showing complete healing or cessation of symptoms, this agent produced best results when given with anticholinergics.*◄

Chymotrypsin (supplied as aqueous solution for intramuscular injection) is an endopeptidase fractioned from the bovine pancreas. It is chemically distinguished from trypsin by the peptide bond it splits. Pharmacologically, it causes a reduction of edema, either by restoring fluid balance in the lymph and venous channels or by removing soft fibrin or inflammatory plugs, thus hastening absorption by greatly increasing tissue permeability. By reversing inflammatory processes the enzyme consequently prevents further necrosis of tissues, in this way enhancing local regeneration and repair.

Material and Method of Study

While chymotrypsin aqueous was being administered to a patient for the treatment of a stasis ulcer, an associated ulcerative colitis subsided unexpectedly, suggesting that the enzyme might be effective in a variety of disease conditions. Successful management of six succeeding cases of severe ulcerative colitis with the enzyme led to its trial in 78 patients with peptic ulcer. These patients were divided into two groups:

GROUP 1 included 24 cases of gastric, duodenal or marginal ulcer in which chymotrypsin aqueous was the only medication employed. Of these patients, 22 were men and 2 women. Their average age was 40.5 years. Initial dosage of chymotrypsin aqueous was 5000 units injected deep into the gluteus muscle daily for 21 days. During the next three to six weeks, 2500 units were administered daily, followed in certain

cases by administration of 5000 units every three or four days for four to eight weeks.

GROUP 2 included 54 cases in which chymotrypsin aqueous was used in conjunction with other medicaments, including propantheline bromide (Pro-Banthine), prochlorperazine (Compazine), antacids, and milk-protein and vitamin supplementation. Of these patients, 46 were men and eight women. Their average age was 42.7 years. The majority were confined to the hospital because of persistent intractable bleeding or because of some obstructive phenomenon such as uncontrollable regurgitation or vomiting. In the majority conventional treatment had not been successful, and in some drastic measures such as daily intubation of the stomach had produced little if any improvement.

A control group consisting of 26 patients (23 men and three women, average age 39.3 years) were treated only with Pro-Banthine in dosages ranging from 60 to 270 mg. daily. Patients in all three groups were placed on ulcer diets and instructed to stop smoking.

Criteria for selection of patients in these three groups included proof of intestinal hemorrhage, or (in the absence of such proof) roentgenologic demonstration of an ulcer crater or niche. Criteria employed in evaluating results were complete cessation of signs and symptoms, supported by roentgenologic evidence demonstrating repair or filling-in of the crater or niche. Such supportive evidence had to be encountered repeatedly while the involved portion of the stomach or duodenum and the adjacent portion of the intestine were in a quiescent, nonirritable state. Insofar as possible roentgenologic studies were performed on the twenty-first, ninetieth, one-hundred and twentieth and one-hundred and eightieth days of treatment.

Results

GROUP 1: Cessation of all symptoms and complete healing of the ulcer occurred in 21 patients (87.5 per cent). The average time required for cessation of symptoms was 5.8 days, that for complete healing as revealed by roentgenologic examination, 24 days. During a period of follow-up observation lasting for from 18 to 33 months, the ulcer recurred in three patients (12.5 per cent) after having remained healed for an average of 8.2 months.

GROUP 2: All symptoms disappeared and complete healing of the ulcer occurred in 49 (90.7 per cent) of the patients in this group. The average time required for the cessation of symptoms was six days, that for complete healing of the ulcer as disclosed by roentgenologic examination, 36 days. The ulcer never healed in two

(3.7 per cent) and healed but recurred in 3 (5.5 per cent) after treatment had been discontinued for an average period of 10 months.

In the control group treated only with Pro-Banthine, 13 (50 per cent) experienced cessation of all symptoms and complete healing. The average time required for cessation of symptoms was 6.4 days, that for complete healing as disclosed by roentgenologic examination, 51.2 days. All 13 healed cases relapsed after treatment had been discontinued for an average of 11.1 months. Chymotrypsin aqueous, subsequently employed in five of these cases, produced complete healing in every case.

Untoward Reactions

Of 4666 injections of chymotrypsin aqueous made during the study, only three (0.06 per cent) produced untoward reactions. Two of these occurred in men and were typical drug allergies manifested by dermal rash, hyperemia, urticaria and itching, one occurring with the eighth and the other with the 46th injection. Both were easily controlled with antihistaminic drugs. The third reaction was an anaphylactic shock episode occurring in a woman and controlled by the intravenous administration of aminophylline, the intravenous and intramuscular administration of anthistaminic drugs, and the administration of ACTH.

Results obtained in this study suggest that chymotrypsin aqueous represents an effective agent for the treatment of peptic ulcer. The concomitant use of anticholinergic and tranquilizing agents is recommended since it enhances the healing properties of chymotrypsin by affording rest to the involved portion of the stomach.◀

Postgrad. Med., 26:542-550,1959.

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Thus Robitussin increases the probability that a cough will achieve its natural purpose—i.e., to remove irritants such as exudates and mucus from the respiratory tract.[1,4,5]

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Diabetes Mellitus: Management with Phenformin, an Oral Hypoglycemic Agent

SAMUEL J. N. SUGAR, M.D.,
LAWRENCE J. THOMAS, M.D., *Washington, D. C.*
TEODORA M. EUGENIO, M.D., and
SERKIS TATLIER, M.D., *Cheverly, Maryland*

►*The response of 47 hospitalized and non-hospitalized diabetic patients to an oral hypoglycemic was noted during a study in which control was also attempted through diet and insulin injections. Adequate control was achieved in 65%, including some who had been unresponsive to other oral hypoglycemic agents.*◄

Phenformin (DBI) is a new oral hypoglycemic agent differing chemically from tolbutamide and chlorpropamide in that it lacks a sulfonyl radical. Although its precise mode of action has not been determined, a number of experimental studies indicate that the drug may act by influencing oxidative metabolism, thereby increasing anaerobic glycolysis and decreasing gluconeogenesis from protein. This theory has not been corroborated clinically, and it has been suggested that phenformin may increase cellular utilization of glucose via the hexose monophosphate shunt in adipose tissue or the liver. Still other reports describe the drug as an insulin-supporting or reinforcing compound.

Method of Study

A total of 47 hospitalized patients, outpatients, and private patients were treated for periods ranging from one to seven months. In the hospitalized patients, blood and urine samples were taken to determine keto-acidosis, which, if present, was relieved by injections of regular insulin and parenteral fluid. Later a measured diet was prescribed and control maintained by doses of regular insulin given fractionally according to the results of urinalysis. Phenformin was then added to the regime, the usual initial dose being 25 mg. three times daily before meals. If control was not attained at this dosage level, the drug was increased by 25 mg. increments until a satisfactory response was noted. Dosage

was decreased, usually by decrements of 25 mg., when good control was noted (as manifested by lowered fasting blood sugar and negative urine tests). Although some patients were controlled with as little as 25 mg. daily, the majority required between 75 and 150 mg. daily.

Management with phenformin was considered satisfactory if the average daily fasting blood sugar was substantially reduced (to the region of 175 mg. per 100 ml. or below), and when urine tests showed less than ¼ per cent sugar. When these requirements had been maintained for a period of at least three days, patients were given a supply of medication and discharged, to be followed in the clinic or office. Particular stress on the need for frequent urine tests at home was made, and a written record of the results requested. Non-hospitalized patients were given phenformin on a similar dosage regime and requested to test the urine at home before each dose of the drug. Insulin, when given concomitantly, was reduced in dosage by decrements of 10 units until either no insulin or an optimal amount in combination with a constant dosage of phenformin was attained. All non-hospitalized patients were seen at weekly intervals until management was considered satisfactory, the frequency of visits thereafter being decreased as improvemen progressed.

Results

Of the 47 patients, 30 (65 pe cent) showed adequate contr either on phenformin alone or i combination with insulin at a re duced dosage requirement. Sev eral patients classified as unstabl diabetics showed good response t phenformin, as did 12 (32 pe cent) of 38 previously not con trolled satisfactorily with tolbuta mide and chlorpropamide. Of th 17 patients (35 per cent) not sat isfactorily controlled with phen formin, the reason for discontinu ing the drug in eight was ineffec tiveness, in three nausea and ver tigo, in two nausea, and in on each diarrhea, diarrhea with vom iting, anorexia, and headache an anorexia.

Side effects in order of fre quency were anorexia (six cases) headache and nausea (five cases) diarrhea, drowsiness and aceto nuria without glycosuria (thre cases), vertigo (two cases), an vomiting (one case). These ef fects were frequently relieved b concomitant administration of 2. mg. amphetamine. Acetonuri without glycosuria was usuall associated with lowered blood su gar levels and may represent "starvation ketosis" due to dimi ished carbohydrate intake.◀

M. Ann. District of Columbia, 28:426-431, 1959.

Hepatic Carcinogenesis

ABRAHAM CANTAROW, *Philadelphia, Pennsylvania*

This conference was held at Mercy Hospital, Pittsburgh, on March 4, 1959, with Abraham Cantarow, M.D., professor of biochemistry at Jefferson Medical College of Philadelphia, as the guest participant. One case is presented and geographical factors and laboratory aids are discussed.

This white male patient was 59 years old in 1953 when he was first admitted to the hospital with a chief complaint of pain in the left side of his abdomen and "over his heart." He had had this intermittently for one year. It apparently would begin in the right side of the abdomen and in the epigastrium and radiate to the left side and upward toward the precordial area. The pain would occur two to four hours after eating and last for one-half to two hours, and was accompanied by nausea but not vomiting. He claimed fatty foods would cause nausea and diarrhea. The patient's appetite was good, however, and there had been no loss of weight.

The patient smoked one-half pack of cigarettes daily. He would go on "alcohol binges" which would last for seven to eight days. During these times he consumed large quantities of alcohol. These "binges" occurred on an average of once every six months. The patient lived alone but said he ate well.

Physical examination at that time revealed the liver to be three finger-breadths below the costal margin. It was non-tender with a smooth edge. No other masses or organs were palpable. Large varicosities were present in both legs and many venous telangiectases were also present in the skin of the legs.

Examination of the urine revealed a clear, alkaline urine with specific gravity of 1.005 and negative sugar and protein. Test for urobilinogen was positive in the undiluted specimen. The red blood cell count was 4,180,000, and the white cell count was 4450. Hemoglobin was 12 Gm. The blood urea nitrogen was 9.7 mg.,

cholesterol 2.3 mg., and cholesterol esters 198 mg. per cent. The van den Bergh test was reported as immediate 2.2 mg. per cent, blood sugar was 109 mg. per cent, alkaline phosphatase 5.7 units, and cephalin cholesterol flocculation was 3 plus. Prothrombin time was reported as 89 per cent. A needle biopsy of the liver was performed and the pathologic diagnosis was Laennec's portal cirrhosis.

The patient was placed on a high protein, high carbohydrate, and low fat diet, and brewer's yeast tablets. He improved considerably and was discharged after three weeks' hospitalization.

The patient was seen in the medical clinic regularly after that time. He was hospitalized on three occasions for pneumonia over the intervening years and finally was hospitalized in 1958 because of a chill and low-grade fever associated with increased swelling of his legs and abdomen. Spider nevi were present in the skin of the chest and back. At that time the abdomen was distended and the liver margin was 12 cm. below the costal margin. It felt hard and non-tender. The spleen was not palpable.

The total bilirubin was 6.42 mg. per cent, blood urea nitrogen 10.5 per cent, serum protein 6.3 Gm. per cent with albumin 2.3 and globulin 4.0 Gm. per cent. The prothrombin time was 24 seconds with a control of 13 seconds. Thymol turbidity was 16.4 units, cephalin flocculation was 4 plus and alkaline phosphatase 5.1 units.

While in the hospital the patient experienced epistaxis and lethargy and finally had massive esophageal bleeding into the gastrointestinal tract; he died three weeks after admission.

DR. MARK M. BRACKEN: "At autopsy an advanced stage of Laennec's portal cirrhosis of the atrophic type was found, associated with primary hepatic cancer. The latter was of the hepatoma type and extensive metastases were found throughout both lungs. In addition, the patient had an associated splenomegaly. Death was caused by massive hemorrhage from esophageal varices."

Dr. Abraham Cantarow: "This case illustrates a very intimate relationship between two different diseases. In this respect primary carcinoma of the liver is a unique disease from several standpoints. Dr. Paul Steiner recently emphasized the fact that because primary carcinoma of the liver is a unique disease, it offers approaches to the study of malignancy that are not offered by most other types of cancer. One of the unique features is the striking variation in the incidence of

primary carcinoma of the liver throughout the world, both in different racial groups and in different geographic situations. Second, it differs from most other types of malignancy in that it is very frequently closely related to the presence of another disease, namely, cirrhosis. Third, it is unique because it may be produced readily in experimental animals by a number of well-known agents, and it also occurs spontaneously in certain experimental animals. Finally, it is unique because of the difficulties which are inherent in the understanding of the clinical nature of the disease and, from many standpoints, in the histogenesis of the different cell types that may occur.

"The clinical diagnosis of hepatic carcinoma presents unusual difficulties, especially in an area such as the United States where the frequency of primary carcinoma of the liver is so low that its presence is usually unsuspected. Almost invariably its clinical manifestations are overshadowed by the presence of far-advanced cirrhosis of the atrophic type. Frequently the diagnosis is not made until the time of autopsy. If one is going to make a diagnosis of primary carcinoma of the liver in a patient who has cirrhosis, he must have some understanding of the duration of the cirrhosis before the diagnosis of the possibility of malignancy can be entertained. The longer a patient lives with cirrhosis, the more likely he is to have a malignancy. The recent increase in frequency of primary carcinoma of the liver in this country can probably be explained in part by the fact that patients with cirrhosis are living longer because of better medical management.

"The time of onset of jaundice and ascites can be very useful criteria in an estimation of the duration of life expectancy. After the onset of jaundice the mortality increases enormously. Less than 30 per cent of patients live for one year after the onset of jaundice and only about 10 per cent are still alive five years later. Similar statistics pertain to the development of ascites. Approximately 35 per cent of patients live for one year after the onset of ascites, and less than 10 per cent are still living five years after the onset.

"The serum bilirubin concentration is increased long before a patient may become visibly jaundiced. The methods of determining serum bilirubin concentration which are used today are quite precise. We assume that the serum bilirubin concentration is within normal limits if it ranges from 0.1 to 1 mg./100 ml. The serum bilirubin concentration in any normal individual remains quite constant. It therefore be-

comes important to know whether a serum bilirubin concentration at any given level is normal for any particular individual. Thus, if one estimates a serum bilirubin concentration at 0.8 mg., there is a 50 per cent chance that this is an elevated serum bilirubin for that particular individual. This illustrates the difficulties that are encountered in the interpretation of values which have such a wide range of normal variation. It is therefore important to appreciate the fact that this range is not a range of normal in any one individual but is the range of normal in the general population.

"It becomes important in the early diagnosis of cirrhosis to know, if possible, whether the serum bilirubin concentration which is within normal limits is actually normal for this particular individual. Cirrhosis may remain latent from a functional standpoint for a long time because of the simultaneous development of hyperplasia in association with the cirrhotic process. In an accumulated series of several hundred cases of cirrhosis, 70 per cent had a normal total serum bilirubin concentration at the time they were first seen. Of this 70 per cent, 28 per cent had an abnormal one-minute direct-reacting bilirubin. To me this is an indication that 28 per cent of these patients probably actually had an increased total bilirubin, but we were not able to interpret it as abnormal because it was within the limits of normal. The bromsulphalein test was abnormal in 43 per cent of the 70 per cent who originally had serum bilirubin concentrations within normal limits. We therefore have at our disposal these two aids in the interpretation of the serum bilirubin concentration — the one-minute direct-reacting bilirubin and the bromsulphalein test.

"If we study all of the examinations that are made in these patients at different times in the course of their disease, we find that the total bilirubin concentration is normal in only 30 per cent of the cases. Of these, there is an abnormal one-minute direct-reacting bilirubin in 33 per cent and an abnormal bromsulphalein test in 70 per cent. Thus, if these three procedures are studied together, one finds that the incidence of normal reaction by all three procedures falls to a very low level in patients with cirrhosis. This is one of the most valuable groups of function tests in the early diagnosis of cirrhosis.

"The presenting symptoms in patients with primary carcinoma of the liver are exactly what one might expect to find in patients with cirrhosis of the liver. Therefore, one must depend upon a few of the unusual things that are

more or less characteristic of primary carcinoma of the liver in suggesting this diagnosis in a patient who is known to have cirrhosis. One of these is the development of an unusual palpable mass which protrudes from the liver. Another time to be suspicious is when a previously atrophic liver begins to enlarge or when pain and tenderness develop in a patient who has not had it previously with the cirrhosis. If the clinical condition deteriorates rapidly and the patient becomes cachectic, this suggests malignancy and the presence of metastases. Hemorrhagic ascitic fluid is present in approximately 50 per cent of all cases of primary carcinoma of the liver.

"From the standpoint of diagnostic procedures, one of the determinations that is becoming more popular is the serum mucoprotein determination. In uncomplicated cirrhosis the serum mucoprotein level is low, while in malignancy of the liver it is high. This is one of the few tests that really shows a striking difference between an uncomplicated cirrhosis and a cirrhosis complicated by malignancy. If there is a disproportionately high alkaline phosphatase level with respect to the level of serum bilirubin, one should be suspicious of malignancy. However, this disproportion is not invariably present, as is shown by the case presented today. Many patients with cirrhosis have an elevation in alkaline phosphatase and many do not. However, if one finds a serum bilirubin concentration which is only slightly elevated and an alkaline phosphatase which is markedly elevated, one should become suspicious of malignancy of the liver. In uncomplicated cirrhosis, the glutamic oxalacetic transaminase level ranges up to approximately 300 units. With a complicating malignancy this may rise to 1000 or even as high as 2000 units. As a rule, the glutamic pyruvic transaminase is not greatly increased in malignancy and the use of these two tests may be of some aid in differential diagnosis.

"The French clinicians in West Africa attach a considerable amount of diagnostic importance to the x-ray visualization of the contour of the diaphragm after the introduction of 1500 ml. of air intraperitoneally. The growth of the tumor upward might distort the normal outline of the diaphragm and the presence of tumorous adhesions to the diaphragm may prevent the air from passing between the liver and the diaphragm to produce the normal pattern. In areas such as French West Africa, where carcinoma of the liver is prevalent, needle biopsy of the liver is rou-

tine for the ultimate diagnosis.

In the United States, approximately 5 per cent of patients with cirrhosis have primary carcinoma of the liver. In terms of total autopsy incidence, primary carcinoma of the liver is found in one-tenth to two-tenths per cent of all autopsies. This is in sharp contrast to figures from Equatorial Africa, where as many as 80 per cent of all patients with cirrhosis may have a superimposed primary carcinoma. Primary carcinoma of the liver is more common in males than in females, but the incidence of cirrhosis of the liver is not much different in males than females. The corollary to these statements is that men with cirrhosis are more likely to get primary carcinoma than women with cirrhosis. This is true particularly of the hepatic-cell type, which is the type found in the patient under discussion today. A similar sex variation in the development of malignancy is seen in rats given certain hepatic carcinogenic agents. In the rats, one can increase the incidence of malignancy in females by administration of androgen in association with the carcinogen. In this country at least, cirrhosis is present in 90 per cent of patients with the hepatic-cell type of liver carcinoma. This means that in 10 per cent of the cases the carcinoma arises in a liver that is not cirrhotic. It is extremely important to recognize this fact, because in the past too frequently cirrhosis was regarded as a necessary antecedent of malignancy. There was also a time when it was believed that antecedent hyperplasia of a tissue made the tissue more susceptible to the development of malignancy. There is evidence that this is not necessarily the case, and whether hyperplasia ever in itself leads to malignancy is certainly an open question.

"The diagnosis of primary malignancy of the liver is almost never made in this country in the absence of cirrhosis, because of its low incidence. The situation in other parts of the world is entirely different, and this is one of the things that may contribute a great deal to our understanding of the nature of carcinoma of the liver. Three years ago, I was fortunate enough to be invited to participate in a discussion in Equatorial Africa with people interested in various types of liver disease and particularly malignancy of the liver. There we had an opportunity to see at first hand the problems that presented themselves. The one disease that is always thought of first across Equatorial Africa when a patient comes into the hospital with abdominal pain and swelling is primary carcinoma of the liver. One of the hospitals in Dakar averages about two new

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References: 1. Ayd, F. J., Jr.: Bull. School Med., Univ. Maryland 44:29, 1959. 2. Azima, H., and Vispo, R. H.: A.M.A. Arch. Neurol. & Psychiat. *81*:658, 1959. 3. Lehmann, H. E.; Cahn, C. H., and de Verteuil, R. L.: Canad. Psychiat. A.J. 3:155, 1958. 4. Mann, A. M., and MacPherson, A. S.: Canad. Psychiat. A. J. 4:38, 1959. 5. Sloane, R. B.; Habib, A., and Batt, U. E.: Canad. M.A.J. *80*:540, 1959. 6. Straker, M.: Canad. M.A.J. *80*:546, 1959. 7. Strauss, H.: New York J. Med. 59:2906, 1959.

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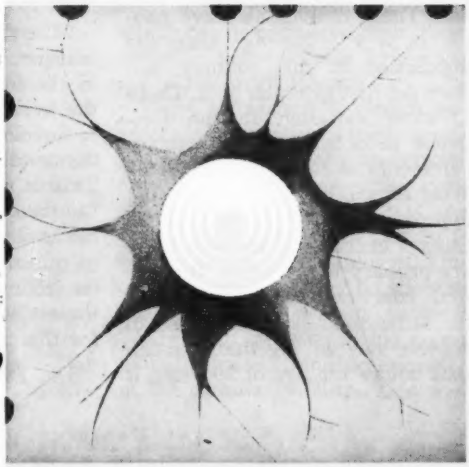

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cases a week. This high incidence occurs not only in Equatorial Africa but also in South Africa, in certain parts of South America, and in Asia. The incidence ranges to as high as 80 per cent of all carcinomas in some areas.

"This very high incidence of hepatic cancer offers an unusual opportunity for the study of possible causes of primary carcinoma of the liver. Although there is a high incidence of cirrhosis in these countries, the incidence of malignancy is proportionately much greater, so the incidence of malignancy cannot all be attributed to cirrhosis.

"Very few natives in Central Africa live beyond 45 years of age. Only 10 per cent of the population is over 45. The average age at death in the hospital population is 30 years for people who have lived beyond 10 years of age. These individuals have cancer at a younger age than the population in this country, but they get just as much of it. There is some variation in the incidence of occurrence of primary carcinoma of the liver in French West Africa, but one can say that approximately 40 per cent of all cases of cancer that are seen there are primary liver cancer. It is the most common cancer in men, and the same holds true in women to a lesser degree. By that, I mean that before the age of 30 years it is the most common type of cancer in women and as the women grow older the incidence of cancer of the breast and uterus exceeds that of hepatic cancer. An interesting observation is that, among the African negroes, 5 per cent of all breast cancers are in males. This is very high when compared with the incidence in the United States. This is believed by some to be a reflection of hepatic disease which occurs in early life among most of these natives, who develop consequent changes in their endocrine status in the direction of feminization. They have skeletons which are indistinguishable anthropologically from women. Their hair distribution is of the feminine type, and their skin is soft and of silky texture. The incidence of gynecomastia is quite high as is the incidence of carcinoma of the breast.

"The fact that there is such an enormous geographic difference in the incidence of carcinoma of the liver provides an opportunity to develop an approach to an understanding of its pathogenesis. This is purely academic at this time and certainly has no practical implications. However, it raises questions such as whether the environment or the constitution of these individuals is responsible for this increased incidence."

DR. BRACKEN: "The incidence

of primary carcinoma of the liver in the American negro is much lower than it is in the African negro. Would that influence your thoughts in regard to constitutional factors having an effect on the development of cancer, Dr. Cantarow?"

DR. CANTAROW: "The geneticists who have analyzed the background of the American negro and negroes in other parts of the world who came from the same racial stock as some of these concluded that there was no evidence of any genetic basis for this difference in susceptibility. The incidence of primary carcinoma in negroes in this country is the same as it is in whites in this country, and the feeling was the environmental factors are probably more important than anything to do with genetics. By constitution I mean changes in the biology of the individual as a consequence of nutritional changes early in life. These experiences early in life may change some of their biologic standards. For instance, they all tend to have low serum cholesterol levels and the incidence of many diseases is entirely different. Coronary occlusion is almost unknown and primary endocrine diseases are unusual."

DR. ERNEST A. FALVO: "Were electrophoretic patterns of serum performed on these patients?"

DR. CANTAROW: "Yes. The characteristic change seen in cirrhosis was present. However, there is nothing characteristic of malignancy when it is superimposed on the cirrhosis, so we derive very little help from the serum protein patterns."

DR. FRANK J. LUPARELLO: "Is there any relationship between nutritional siderosis and hepatic cell carcinoma? In this country we know that the incidence of hepatic carcinoma is greater in hemochromatosis."

DR. CANTAROW: "According to the statisticians, there appears to be a closer relationship between the duration of life and the development of malignancy than there is between the nature of the cirrhosis and the development of the cancer."

DR. FRANCIS F. FOLDES: "You mentioned that these patients had low serum cholesterol levels. Do they show any other changes, such as the cholinesterase level, which can be compared with those found in patients with liver cancer in the United States?"

DR. CANTAROW: "I cannot answer this with respect to cholinesterase. Patients having no demonstrable liver disease who were studied showed no evidence of impaired liver function by any procedure which was employed. The only abnormality they do show is in the plasma protein pattern. There is an increase in the aplha globulin fraction and occasionally in the gamma globulin. This was

believed to be a reflection of what had happened to them in infancy. Almost all of these infants develop kwashiorkor in the early months of life. This is a nutritional disease. If the infants do not succumb to it, they apparently get over it completely. Follow-up by yearly needle biopsy of the liver usually shows nothing until suddenly cirrhosis begins to develop. Most of the individuals studying this problem claim that there is no progression into cirrhosis from the disease of infancy. However, some of the men in West Africa feel that they can demonstrate a regular progression morphologically from one disease to the other. After the infants have been exposed to the insult to their liver, endocrine changes develop which are a consequence of the liver disturbances and the protein pattern changes. If one determined "biologic standards" for a presumably healthy African negro in his teens, they would be different from those of the average European or the average American. They would be his normals, but the important question is whether they are his normals genetically or whether they are his "normals" because of the consequence of nutritional disturbances to which he has been exposed. An important question is whether this background of liver disturbance in early life makes it possible for some carcinogen in the environment to which he is exposed in later life to hit him with greater frequency than in the European population which has not been exposed to similar insults."

DR. BRACKEN: "Dr. Cantarow, at this time would you say a few words on the interpretation of the serum bilirubin estimation? We are using the Evelyn method for the determination."

DR. CANTAROW: "The Evelyn method is perfectly satisfactory for total bilirubin. The difficulties arise in interpretation. We must accept as normal any bilirubin concentration that ranges between the limits of 0.1 mg. and 1 mg. per 100 ml. There are occasional normals that are as high as 1.2 mg. This is a range of normal in the general population and it represents the serum bilirubin concentration that represents a balance between the rate of hemoglobin destruction and the rate of bilirubin excretion in the bile. The rate of hemoglobin destruction is constant. We do not destroy 100 million erythrocytes one minute and 10 million erythrocytes the next minute. The liver has an enormous capacity for excreting bilirubin. Therefore, as much bilirubin as is being formed will be excreted, even in the presence of somewhat impaired liver function. My approach to the study of the

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excretory function of the liver would be as follows: We have three tests at our disposal—the total bilirubin, the one-minute direct-reacting bilirubin, and the bromsulphalein excretion. If the total bilirubin is abnormally high, there is no necessity for either the one-minute direct-reacting bilirubin or the bromsulphalein excretion test. They give no additional information, except possibly in the diagnosis of hemolytic jaundice. If the total bilirubin is within normal limits, the one-minute direct-reacting bilirubin bilirubin should be used. This can be done automatically by the laboratory without bothering the patient again, because the serum is already available. If this reading is abnormally high, one does not need the bromsulphalein test, for it will not provide additional information. If the one-minute direct-reacting bilirubin is within normal limits, the bromsulphalein test should be performed. If there is some sort of an understanding between clinicians and the laboratory in regard to the handling of these procedures in this fashion, everyone will be spared a great deal of trouble."◀

Pennsylvania M.J., 62:1344-1348,1959.

The Effect of Penicillin on Acute Rheumatic Fever and Valvular Heart Disease

The control of symptoms of acute rheumatic fever is easily attained by several methods of therapy, however, no form of treatment has had a marked effect on acute carditis and valvular heart disease, the two complications that determine the ultimate prognosis. In an attempt to alter the course of established rheumatic fever by removing the original inciting agent, 49 patients with acute rheumatic fever received large doses of penicillin and 48 control patients received no antibiotic.

In this study of 97 patients with acute rheumatic fever, 6 weeks of intensive penicillin therapy appeared to have no effect upon the acute clinical, laboratory and electrocardiographic manifestations. The treatment did appear to produce a reduction of probable significance in the incidence of valvular heart disease a year later. The disparity between the effects on the acute-phase manifestations and those on the endocardial lesions suggests that these may differ pathogenetically. The results indicate that the living streptococcus continues to play a significant part in the development of valvular heart disease, even after symptoms of rheumatic fever have appeared.

It is concluded that an intensive course of penicillin may be important in the therapy of acute rheumatic fever for its effect on valvular heart disease. In addition, symptomatic therapy should be administered to control acute symptoms.

Mortimer, E. A., Jr., et al., *New England J. Med.*, 260:101-112,1959.

Ten Years of Progress in Early Cancer Detection

During the last 10 years there has been steady and marked increase in the percentage of cancers diagnosed at an early stage. The reduction in the death rate from cancer among women is shown most markedly by the 38% decrease in the death rate from uterine cancer. If 34% of present-day cancers are diagnosed while still early, it means that 66% are in groups classified as other than early, and therefore would not have the maximal opportunity for cure. The great increase in the death rate from lung cancer is a sobering fact.

Handy, V. H., & Gerhardt, P. R., *New York J. Med.*, 59:793-796,1959.

Hemoptysis in Older Men

Massive hemorrhage is more characteristic of suppurative disease or tuberculosis than of cancer. Fatal hemorrhage is rare and is usually from rupture of an aneurysm in a tuberculous cavity or an aortic aneurysm into a bronchus.

Hemoptysis has been the most important symptom in relation to lung cancer among 6,137 men over age 45 who report every 6 months for interview and x-ray. Hemoptysis had been experienced by 395 (6.5%); one of 4 had cough for months or years; 5% whose chest x-rays were "negative" reported hemoptysis. Infection accounted for most of the hemoptyses, with neoplasms in second place and cardiovascular disease a close third.

The death rate has been markedly lower for the group of 170 in whom no cause was found for their hemoptyses initially, or on follow-up of one to 5 years. The 18-month mortality rate for the men with hemoptysis was 14%; for those who had not had hemoptysis it was 6%.

Hemoptysis was reported in a lower percentage of non-smokers than of those who smoked and was highest in cigarette smokers. Pipe smokers manifested the symptom significantly more than non-smokers, but were much better off than cigarette or cigar smokers. Only one cancer has occurred in 890 non-smokers—in a man who did not report hemoptysis. Among the smokers, the prevalence of proved cancer has been 5 to 6 times higher among moderate and heavy cigarette smokers with than without hemoptysis. Hemoptysis occurs late in the course of lung cancer.

Boucot, K. R., *Missouri Med.*, 56:27-28,1959.

Quinidine

Quinidine can be used for nearly all types of cardiac arrhythmias with the exception of those due to digitalis intoxication. The most important therapeutic uses are in the conversion of atrial fibrillation and ventricular tachycardia to normal sinus rhythms.

Atrial flutter has been converted successfully to a regular sinus rhythm in from 20 to 30% of conversion attempts. Danger lies in the ventricles responding to each atrial beat instead of a 2:1 or 3:1 atrioventricular block which was present before treatment. It may be well to convert the flutter to fibrillation with digitalis and then convert the fibrillation to a regular sinus rhythm with quinidine. Paroxysmal supraventricular tachycardias can be restored to a normal sinus rhythm with quinidine, 0.4 to 0.6 gm., every 2 to 3 hours until relieved. Sino-atrial tachycardias will not respond to quinidine.

Hilty, D. E., *Missouri Med.*, 56:152-154,1959.

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Current Concepts in Therapy: Sedative-Hypnotic Drugs II. Chloral Hydrate. New England J. Med. 258: 700 (Apr. 7) 1958.

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1 or 2 9¾ gr. capsules or ¼ to 1 teaspoonful of Noctec Solution 15 to 30 minutes before bedtime.
7½ and 9¾ gr. capsules, bottles of 100. Solution, 7½ gr. per 5 cc. teaspoonful, bottles of 1 pint.

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Hearing Impairment: Recognition and Treatment

Congenital deafness may be due to failure of development of certain portions of the cochlea, birth injuries, meningitis, encephalitis or rubella in the mother in the first trimester of pregnancy, or mumps or measles in the child. Children with hearing impairment also exhibit speech defects proportional to hearing loss. If residual hearing is within conversational range, such children can benefit from use of a hearing aid. Lip reading instruction and employment of visual speech methods enable these children to obtain an education and to facilitate their environmental adjustment. In acute middle ear disease in children, administration of antibiotics and drainage when indicated are the most effective methods of treatment. Removal of infected tonsils and adenoids associated with this condition is mandatory, followed by irradiation to destroy residual lymphoid tissue at the orifices of the eustachian tubes not accessible to surgery.

Deafness evident only when conversational range is reached results from long-standing or frequently recurring partial occlusion of the pharyngeal end of the eustachian tube by lymphoid tissue. In some children, especially those with allergy, residual adenoids sometimes become infected and impair hearing. Treatment with radium applicator has proved safe and effective in restoring normal eustachian tube function in this order.

Otosclerosis usually occurs during young adult life, more frequently in women. Hearing in this condition is reduced by air conduction, good by bone conduction. The tympanic membranes and nasopharynx appear normal. A gradual, flat loss of all tones except those of higher frequency occurs in both ears, tinnitus usually in one or both ears. A hearing aid, and fenestration and adjunctive stapes surgery afford a high percentage of relief in these cases.

In patients with Meniere's disease whose hearing has remained serviceable, section of the vestibular portion of the eighth nerve will maintain hearing and reduce vertigo. In ear casualties with irreversible pathologic changes among military personnel and civilians in noisy occupations, lip reading, aural rehabilitation and the use of hearing aids are helpful. Hearing impairment of old age is slowly progressive, principally affecting the higher tones and causing difficulty in identifying speech. Careful fitting of a hearing aid together with intensive counselling of patient and family may be beneficial in these cases.

Lieberman, A. T., *Maryland M.J.*, 8:553-556, 1959.

Surgery of the Pancreatic Ducts in Chronic Pancreatitis

The type of operative procedure depends on the site of obstruction:

1. Obstruction at the Ampulla of Vater. In the absence of intrahepatic obstruction a soft metal probe will traverse Wirsung's duct into the tail of the gland with ease. It is mandatory that the pancreatic duct orifice be located when sphincterectomy is performed for drainage of the pancreas. A small calculus may be removed through this approach using otologic alligator forceps.

2. Stricture in the head or body of the pancreas. If the dilated main pancreatic duct can be palpated, the favored method is a side-to-side anastomosis. When a dilated duct cannot be readily palpated distal pancreatectomy and Roux-Y drainage are the procedures of choice.

3. Diffuse inflammatory disease of the head of the pancreas. The procedure of choice is partial pancreato-duodenectomy. Results are excellent when the islet and acinar tissue of the tail are not completely destroyed.

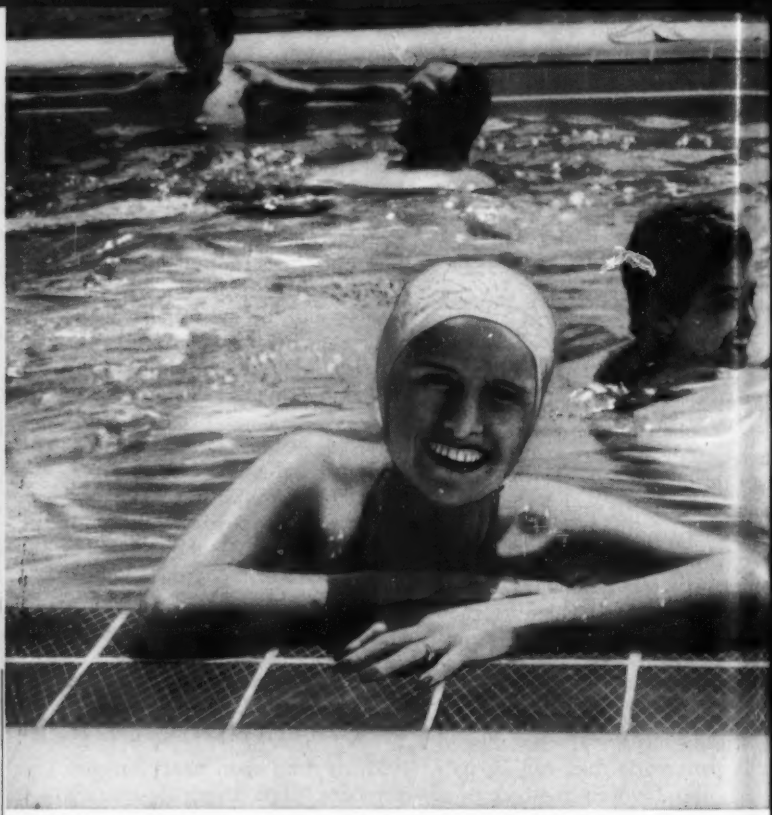
In effecting pancreatic duct anastomosis, all bleeders and ductules are carefully grasped with mosquito forceps and tied with fine silk. The main duct is then isolated and the cut surface of the pancreas inverted around the pancreatic duct. A buttressing row of 5-0 silk is laid posteriorly and anteriorly to proximate the inverted surface of the pancreas to the serosa of the bowel.

Of 36 patients with chronic pancreatitis treated surgically with these methods, 31 showed good, and 5 poor results, with the operative mortality only 2 (7%).

Thal, A. P., *Minnesota Med.*, 42:119-122,1959.

A New Method of Open Heart Surgery

Much good open heart surgery has been done using equipment or methods that are inherently dangerous. It is now time to reexamine methods in this important field and abandon all equipment and procedures that depend primarily on good luck or on the manual dexterity of the surgeon. Highly satisfactory work can be done using well designed pump-lungs that supply all the basal needs of blood flow of the patient. Unfortunately, few centers have such equipment because it is expensive and complicated.



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Pierce, E. C., II, et al., *J. Tennessee M.A.*, 52:39-44,1959.

Treatment of Melanoma by Isolation-Perfusion

The ultimate results of therapy are difficult to evaluate, because these tumors may remain quiescent for long periods of time and metastases may become evident many years after treatment of the primary lesion. The 5-year survival rate, after presumably adequate surgical excision, is 20 to 40%. Radiotherapy has proved ineffectual, and the results with systemically administered nitrogen mustard have been unimpressive.

In order to administer high concentrations of chemotherapeutic agents for the treatment of cancer, a technique of isolation and perfusion of the tumor-bearing area has been developed. Eight patients with malignant melanoma have been treated by this technique. The regression, even disappearance, of neoplastic lesions in these patients indicate that phenylalanine mustard in high concentrations may be effective against melanoma.

When the lower extremity was effectively isolated and phenylalanine mustard was administered in a dose not exceeding 2 mg. per kg. of body weight, serious depression of hematopoiesis did not occur.

Creech, O., Jr., et al., *J.A.M.A.*, 169:111-115, 1959.

Trends in the Surgery of Diverticulitis

Diverticulosis has been reported in 5.2 to 10% of autopsies. The lowered risk of resection of the sigmoid makes it the treatment of choice in an increasing number of cases. One-stage operations are convenient, but multiple-stage operations are still done when in doubt. Often a carcinoma of the sigmoid is treated as diverticulitis, until it is too late to do much about it. Major bleeding from diverticulosis is rare, but does occur.

Patterson, H. A., *J. Kentucky M.A.*, 57:35-41, 1959.

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Gastroscopy and Esophagoscopy: Analysis of 1752 Cases

In 892 gastroscopies in 805 patients and 860 esophagoscopies in 661, usual management included:

1. Withholding of food and liquid after midnight.

2. Premedication with oral barbiturate and topical-anesthetic gargle or (in recent years) with meperidine I.V.

3. Use of lateral decubitus position, with trained technician holding and moving patient's head as instructed by endoscopist.

4. Use of Cameron omniangle flexible gastroscope and Eder-Hufford esophagoscope (with flexible, rubber-tipped obturator).

5. Examination of roentgenograms before endoscopy.

Pathologic lesions found in 434 (48.7%) by gastroscopy included gastritis in 341 and gastric ulcer in 88, while those found in 510 (59.3%) by esophagoscopy included varices in 242, esophagitis in 180 and hiatal hernia in 97. There were no deaths and only three complications (all perforations by esophagoscopy), one requiring surgery.

Recommended indications for gastroscopy include upper gastrointestinal hemorrhage of uncertain source, gastric ulcer (when there is possibility of malignancy or doubtful progress in healing), and gastric abnormalities, evident but not definable radiographically. Indications for esophagoscopy include upper gastrointestinal hemorrhage of uncertain source, dysphagia or other symptoms referable to swallowing or to the esophagus, hepatic cirrhosis or signs suggesting portal hypertension, hiatal hernia with symptoms, and any evidence of esophageal obstruction.

Sullivan, B. H., Jr., & Myers, J. E., Jr., *M. Ann. District of Columbia*, 28:442-476,1959.

Surgery of the Neck After Irradiation for Cancer

In 19 cases of primary laryngeal and 3 of primary pharyngeal carcinoma, indications for surgery included unarrested cancer and severe irradiation reactions not amenable to medical treatment. Analysis of these cases shows that:

1. Within the first year after irradiation therapy for cancer of the larynx, surgery of the neck usually can be done without technical difficulty or undue complications in healing.

2. Radiation changes in these "early" cases of laryngeal cancer present many problems during operation and postoperatively. Some patients had perichondritis of the laryngeal cartilages and were seriously ill despite apparent arrest of the cancer.

3. After the first year following irradiation therapy of the

larynx the surgeon can expect many problems both during the operation and in the postoperative care of the patient, whether or not there is persistent cancer.

4. Inoperable cancer of the pharynx may become operable following x-ray therapy. Technical problems of surgery for pharyngeal cancer are not remarkable. Although healing was not unduly delayed in 2 such cases in the present series, in the third case necrosis of the mandible and fistula of the mouth presented special problems.

Work, W. P., *Ann. Otol. Rhin. & Laryng.*, 50: 393-410,1959.

Unoperated Acute Abdominal Diseases: Follow-up of 137 Cases

The patients were divided into 2 groups, one of 109 persons aged 60 to 85 and the other of 28 persons all under 60. Twenty-three in the older and 11 in the younger group had cholecystitis (acute and with peritonitis in 18 of the older and in 4 of the younger group), 14 in the older and one in the younger group had acute appendicitis, 16 in the older group acute appendicitis with diffuse peritonitis, 35 in the older and 9 in the younger appendiceal abscess, 2 in the older and one in the younger pelvic peritonitis, one in the older sigmoiditis, and 2 in the younger pancreatitis. Patients below 60 with acute appendicitis and diffuse peritonitis were operated on and therefore excluded from this investigation. Of the patients in the older group, 7 (43%) died of acute appendicitis with diffuse peritonitis and 5 (14%) of appendiceal abscess. There were no deaths among patients in the younger group. The decrease in deaths from acute abdominal disease over the past decade is attributable to the use of antibiotics. Results of this investigation indicate that emergency operation for acute cholecystitis is not justifiable.

Parenti, C., *Chir. ital.*, 10:662-647,1958.

ALTAFUR in surgical (soft tissue) infections

In a series of 159 patients with various surgical infections (cellulitis, abscess, wound infections), ALTAFUR was employed with eminently satisfactory results. The incidence and magnitude of surgery were considerably reduced, and when surgical intervention was necessary it could be delayed until the inflammatory process had receded or become localized.

Excellent therapeutic response was obtained in patients with infections due to coagulase positive Staphylococcus aureus, beta hemolytic Streptococcus, and Escherichia coli; these organisms were uniformly susceptible to ALTAFUR in vitro. An insensitive strain of Pseudomonas aeruginosa was isolated from the single patient who failed to respond.

The majority of patients received ALTAFUR 100 mg. four times daily per os.* Duration of treatment ranged from 4 to 30 days, averaged 6 days. There was no clinical or laboratory evidence of toxicity in any case, and ALTAFUR was well tolerated by all but 1 of the 159 patients.

Prigot, A.; Felix, A. J., and Mullins, S.: Paper presented at the Symposium on Antibacterial Therapy, Michigan and Wayne County Academies of General Practice, Detroit, Sept. 12, 1959 (published Nov. 1959).

*Experimental dosage (see dosage recommendations adjacent)

Treatment of Idiopathic Thrombocytopenic Purpura

Of 93 (28 male and 65 female) patients, 26 had no specific treatment and were given hematinics or transfusions of whole blood. Of the remaining 67, 31 had specific treatment beginning less than 100 days after onset of symptoms, and 36 specific therapy beginning on a later date. Specific treatment was with ACTH, cortisone or prednisolone in 19 of the 31, and in 8 of the 19 there ensued complete remission which was maintained after treatment was stopped. There was a tendency to spontaneous remission in patients with a short history, and onset of such remissions seemed to be hastened by steroid therapy. Of the 23 with a long history given steroid therapy, distinct improvement was shown in 12, but this was not maintained for more than 60 days in any instance. Twelve of the 31 with a short history who did not receive steroids, and 7 who failed to benefit from them were treated by splenectomy. Of the 36 patients with a long history, 33 were treated by splenectomy (14 of the 33 had received steroids). Splenectomy was followed by good results in more than 75% of those with a short history in whom no remission, spontaneous or induced had occurred. Splenectomy was followed by good results in 50 to 60% of the patients with a long history.

Watson-Williams, E. J., et al., *Lancet*, 2:221-226,1958.

Comparative Effectiveness of Codeine Phosphate and Dextro-Propoxyphene Hydrochloride

Dextro-propoxyphene hydrochloride (DPH) was synthesized in 1953 in an effort to find a nonnarcotic analgesic. The product was employed in 140 patients, comparing it with codeine phosphate mg. for mg. The diagnoses were post partum 90, orthopedic cases (fractures and herniated intervertebral disks) 11, pulmonary disease (pneumonia, pulmonary infarction and empyema) 14, malignant tumors (all metastatic) 14, and 11 miscellaneous.

The remaining 50 patients who were not post partum were given the drugs for a minimum of 8 days, the same drug for 3 consecutive days. Most patients were on a 4 times daily or on an every 4 hour dose schedule. Some receiving the 64 mg. doses for cancer were treated for long periods

and eventually were given only DPH. In several instances a dose of 128 mg. 4 times daily was used with no side effects. The reasons for discontinuing the use of codeine phosphate were the constipating effect of the 64 mg. dose and the fact that DPH can be given with increasing doses above 64 mg. with increasing analgesia, which is not true of codeine.

Dextro-propoxyphene and codeine phosphate hydrochloride appear to be equal in analgesic properties. On the 64 mg. regimen, DPH causes less constipation and fewer central nervous system symptoms than does codeine phosphate, and exhibits an increased analgesic effect (without significant side reactions) when the dose is raised above 64 mg.

Wilson, W. L., et al., *Pennsylvania M.J.*, 62: 186-187,1959.

Nasal Decongestion with a New Oral Preparation

A total of 35 patients, aged 25 to 50, were treated with a new nasal decongestant agent in oral form (Nolamine), each timed-release tablet of which contains chlorprophenpyridamine maleate 4 mg., phenindamine tartrate 24 mg., and phenylpropanolamine hydrochloride 50 mg. Dosage was one tablet every 10 to 12 hours for a period of 12 days, this course of therapy being repeated once in three patients and twice in one patient. The major consideration for inclusion of a patient in this series was the presence of nasal congestion, regardless of cause. Only those not having received immediate previous therapy were selected. Adjunctive measures employed in some of the patients included administration of local and/or systemic antibiotics.

Therapeutic response was tabulated as follows:

1. Treatment was considered a failure in two patients (5.8 per cent).

2. Six patients (17.1 per cent) showed fair improvement.

3. Twenty-seven patients (77.1 per cent) exhibited favorable to highly satisfactory results.

The drug combination was equally effective whether nasal congestion was associated with the common cold, sinusitis, rhinitis, nasopharyngitis, or hay fever or other allergy. Eustachian salpingitis as well as postnasal drip was also relieved in some patients. A number of those receiving the initial dosage of the medication in the office showed objective signs of nasal decongestion after 20 to 30 minutes. The only side effect reported was general malaise in one patient, this clearing when the medication was discontinued. Adverse reaction of the nasal mucosa or rebound congestion did not occur.

Schwartz, T. A., & Slasmaan, W. H., Jr., *Eye Ear Nose & Throat Month.*, 38:645-648, 1959.

Rhinitis Treated with a Drug Combination

The majority of 35 patients receiving a new preparation for the treatment of allergic and chronic rhinitis reported improvement. This new drug form (Rynatan) combines pheynylephrine, prophenpyridamine, and pyrilamine in a new principle providing sustained release despite changes in gastric motility or pH, and is available in tablet or suspension. Each of 17 patients treated at a clinic received one tablet and were observed for one hour for possible side effects, then given a two days' supply on a schedule of 1 tablet t.i.d. Medication was continued for one week and the patient examined, then discontinued for two weeks and the patient reexamined. The suspension form was administered to 18 children on the dosage schedule of one teaspoonful two to four times daily for two weeks, during which time regular evaluations were made. Patients were examined one week following after the drug was discontinued. Slight shrinkage of the nasal mucosa was noted by most patients during the first hour following administration. Side effects were not noted, although four children exhibiting minor anorexia during therapy regained their appetites when the medication was discontinued.

Villanyi, L., & Stillwater, R. B., *E.E.N.T. Month.*, 38:650-651,1959.

Chemotherapy for Depression

A preparation combining a tranquilizer and a central parasympathetic suppressant (Deprol) was used as an adjunct to psychotherapy for 87 severely depressed psychoneurotic patients. Each tablet contains 400 mg. meprobamate and 1 mg. benactyzine hydrochloride. Usual starting dosage was 1 tablet 4 times daily, increased as indicated to as many as 8 daily. For depression accompanied by severe anxiety and agitation or by intractable insomnia, 1 to 3 400-mg. tablets of meprobamate were added during the day and 1 to 2 at night. This therapy was effective—without depressing appetite or inducing euphoria—in controlling anxiety, tension, sleep disturbances, and psychosomatic complaints, and was particularly effective in patients with pronounced depressions characterized by apathy, retardation, withdrawal, and inability to perform. All but 2 of the 87 patients were benefited. There were no side effects from prescribed doses, and from massive doses (30 to 40 tablets) taken by 2 patients in attempted suicide, only prolonged sleep with transient fall in blood pressure. This combination of drugs safely and effectively treats depression, especially that characterized by retardation and anxiety.

Ruchwarger, A., *M. Ann. District of Columbia*, 28:438-441,1959.

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- Tinea pedis improves in 1 to 2 weeks; complete clearing may require 3 to 6 weeks.
- Tinea capitis improves in 2 to 3 weeks; is usually cured in 3 to 5 weeks.
- Onychomycosis (tinea unguium) — fingernails clear in 3 to 4 months; new normal growth is seen earlier; toenails require longer treatment.
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Literature concerning method of administration and dosage is available upon request.

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Reversal of Cardiac Edema with Prednisone

A total of 10 patients under treatment 2 or more years for persistent congestive heart failure were given prednisone, 2.5 mg. daily, increased to 15 to 20 mg. daily for 4 or 5 days, then gradually decreased depending on response to a mercurial given after the priming doses with prednisone. The daily maintenance dosage was 2.5 to 10 mg., averaging 5 mg. In 2 patients the initial dosage attained a daily maximum of 35 mg. All patients had become unresponsive to the usual diuretic measures, including mercurials and attempts at induced hyperchloremia and acidosis. Possible contradictions to steroid therapy were considered in each case prior to therapy. Prednisone was not administered routinely but as an adjunct to other measures.

Refractoriness was reversed in 8 on this regimen. Possible explanation of the mechanism of this reversal is the promotion of transcellular and transcompartmental shifts of electrolytes from an electrolyte pool. Although the basic cardiac disease is not arrested by this measure, a grace period of months or even years may be obtained, after which time standard treatment may be reinstituted to maintain adequate compensation.

Newman, D. A., *New York J. Med.*, 59:625-633,1959.

Acne: Treatment with An Antiseptic Lotion

Bithionol is active in low concentrations against common bacterial and some fungal skin contaminants. It is not irritating nor sensitizing and has a high degree of "substantivity" (capacity to leave a residue adhering to the skin).

A lotion containing bithionol 1%, dispersible sulfur 5%, zinc sulfate 3%, and zinc oxide 10% in a non-greasy flesh-tinted base (Acnederm) was used in 374 patients, 306 of whom were diagnosed as having acne vulgaris, in 24 rosacea, 21 seborrheic dermatitis, 15 tinea corporis, 7 tinea versicolor, and 1 seborrhea oleosa facialis.

Patients were instructed to cleanse the skin with a mild soap and to apply the lotion several times daily and at bedtime, each time allowing the lotion to dry and removing the excess with a dry puff or tissue.

Of 4 patients failing to respond favorably, 2 had acne, 1 rosacea, and 1 tinea corporis. Contralateral paired controls demonstrated that inclusion of the antiseptic lotion contributed materially to the benefit obtained.

No untoward effects were noted, and the lotion proved cosmetically acceptable.

Niedelman, M. L., *Am. Pract. & Digest Treat.*, 10:1001-1003,1959.

Thrombocytopenia During Chlorothiazide Therapy

Chlorothiazide appears to decrease circulating platelets in about 1% of patients receiving the drug, this effect being confirmed in *in vitro* studies. The reaction is usually brief, the platelet count returning to normal on withdrawal of the drug. It is considered desirable to make a blood cell count when chlorothiazide is given to older or debilitated patients, or when it is combined with other drugs capable of depressing the hematopoietic system. Of 6 patients developing thrombocytopenia during treatment with chlorothiazide, 3 also developed a purpuric rash. No additional blood manifestations were observed.

Nordquist, P., et al., *Lancet*, 1:271-272,1959.

Phenethylbiguanide (DBI) Orally in Diabetes

DBI is a synthetic nonsulfonylurea compound effective orally as a hypoglycemic and hypoglycosuric agent in diabetes mellitus. The mechanism of its action has not been established. It does not influence blood sugar levels of non-diabetic persons, and for successful management of diabetes appears to require the presence of exogenous or endogenous insulin. Though there is no evidence of cumulative action, therapeutic response may not be clearly evident for several days. It was given, alone or with insulin, to 206 unselected patients for a period of 24 months. Maximum initial daily dose was 50 mg. Close observation determined each successive step in gradually decreasing insulin and increasing DBI until maximum dosage (200 mg. per day) was achieved. Only 2 patients were given more than 150 mg. of DBI daily. Prescribed diets ranged from 1200 to 2200 calories per day, with (except for those above 1800 calories) daily intake of protein kept at 70-80 gm. and of carbohydrate at 150 gm.

DBI was discontinued in 53 cases (26%) because of gastrointestinal side effects and in 25 others (12%) for reasons not related to effectiveness or side actions of the drug. In the remaining 128 cases (62%), DBI proved clinically useful without insulin in 110 (53%) and with 50% reduction in insulin in 18. The sole limitation to use of DBI appears to be its gastrointestinal side effects, the incidence of which was reduced late in the series by improved dosing techniques. Results of therapy appeared not to be related to age, age at onset, duration of diabetes, nor duration of insulin therapy. There was no evidence of organ toxicity nor of secondary resistance to the drug.

Pomeranze, J., et al., *J.A.M.A.*, 171:252-258, 1959.

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Vitamin D	*800 U.S.P. Units*	*1,000 U.S.P. Units*
Thiamine HCl (B_1)	*1.5 mg.*	*1 mg.*
Riboflavin (B_2)	*1.5 mg.*	*0.8 mg.*
Pyridoxine HCl (B_6)	*1 mg.*	*1 mg.*
Ascorbic Acid (C)	*40 mg.*	*50 mg.*
Vitamin B_{12}	*3 mcgm.*	*1 mcgm.*
Niacinamide	*10 mg.*	*10 mg.*
Pantothenic Acid (as Panthenol)	*1 mg.*	*2 mg.*
Methylparaben	*0.08%*	*0.08%*
Propylparaben	*0.02%*	*0.02%*

Doctors and the Law

CHARLES J. FRANKEL, M.D., L.L.B., *Editor*

►*Can a doctor be found guilty of malpractice, for alleged negligent manipulation of patient's neck during operation, when patient, whose cause of death on the operating table was given as "heart arrest," was found, at the mortuary, to have a fractured vertebra and crushed spinal cord?*◄

This question was passed on in *Guest* vs *Breedin*, 257 F. (2d) 22 (C.A. 4, 1958). The patient had suffered from osteoarthritis for ten years. The disease had progressed so far that his spine was curved almost to a half circle and wryneck drew his head down to the left. Defendant anesthetized the patient in order to examine his neck muscles in a relaxed state to determine whether surgery to relieve the wryneck was justifiable and, if it was justifiable, to proceed with the operation. Defendant and some nurses who were present at the operation testified that defendant manipulated the patient's neck gently. However, one nurse testified that while defendant was manipulating the patient's head and neck, the patient "rared his legs" against the strap holding him to the table. After examining the patient for an hour, defendant decided the operation was too big to be done at that time. Immediately thereafter the patient's pulse disappeared suddenly and he died within a short time.

A relative who visited the mortuary that afternoon discovered the decedent's head could be moved from side to side. The funeral director testified that no act of violence was performed on the body at the mortuary. To fit the body into the casket it was "adjusted" by leveling the legs and head to equal heights, with supports under them.

A pathologist and a radiologist who performed an autopsy the next day found that the third cervical vertebra was fractured and that this had crushed the spinal cord. There was also evidence of hemorrhage in the area and they testified, on the basis of the character and extent of the hemorrhage, that the spinal cord was

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crushed before death and that this was the cause of death.

Doctors who testified for plaintiff stated it would have taken considerable pressure to break the neck bones. Defendant admitted that the use of sufficient pressure to break the neck would have been gross negligence and contrary to all standards of medical treatment, and that the deceased's bones were not abnormally chalky or brittle. He contended he had not applied excessive pressure and that the patient must have died from a "heart arrest" which would not show in the autopsy. Defendant argued that deceased's vertebra must have been broken by the people at the mortuary when they tried to "adjust him and that the hemorrhage must have been caused by the force of the embalming fluid. The pathologist and the radiologist testified that what they found in the autopsy could have been caused only by the action of the heart and not after death in the embalming process. The Court said that the evidence was sufficient to support a finding by the jury that defendant was guilty of malpractice.

►*Can an osteopath be deprived of staff and hospital privileges without being notified of charges against him and without a hearing?*◄

This question was before the Supreme Court of Pennsylvania in 1959 (*Berberian* vs *Lancaster Osteopathic Hospital Association, Inc.*, 149 A. (2d) 456). Plaintiff had been a member of the staff of defendant hospital since 1948. In February, 1958, following plaintiff's arrest on a charge of conspiracy to commit abortion, he was requested to resign from the staff but he refused to do so. In March, 1958, the staff executive committee held a meeting to determine whether to recommend plaintiff's dismissal from the staff because of the abortion charge; plaintiff attended the meeting with counsel. The committee decided to make no recommendation pending final legal disposition of the abortion charge; plaintiff was never indicted on the charge. The day after the committee meeting the hospital's board of directors held a meeting at which they requested the hospital's medical director to prepare a report concerning plaintiff. In April, 1958, the board of directors and the staff executive committee met to consider the medical director's report. Plaintiff received no notice of this meeting and did not attend. The report charged plaintiff with grossly unprofessional and criminal conduct. The board of directors, on the basis of the report, voted to deprive plaintiff of all staff privileges and the use of the hospital's facilities.

The Court said it was obvious that plaintiff will suffer irrepar-

able harm unless the hospital is enjoined from depriving him of staff and hospital privileges because the nearest osteopathic hospital, other than defendant, is 30 miles away. However, the only question for determination is whether plaintiff was legally entitled to a hearing on the charges in the medical director's report before being dismissed. The general rule is that the directors of a private hospital may, at their discretion, remove a doctor from its staff. However, a private hospital must give a doctor a hearing before removing him from its staff if its duly approved constitution or by-laws so provide; the constitution and by-laws are a contract between the hospital and the staff members. Thus, defendant hospital's constitution and by-laws must be examined to determine the exact nature of the contractual relation between plaintiff and the hospital.

The hospital's by-laws provide that the directors may deprive any staff member of his hospital privileges. However, the directors have also approved the staff's by-laws which provide that the staff executive committee has the right to recommend the suspension of a staff member to the directors, but only after adequate hearing and a thorough investigation. The by-laws further provide that a doctor who is suspended has a recourse to appeal, with legal counsel, before a joint meeting of the staff executive committee and the board of directors. When the board of directors approved the staff by-laws, they became an integral part of the contractual relation between the hospital and its staff members. Therefore, said the Court, defendant may deprive plaintiff of staff privileges and use of hospital facilities only after a hearing duly held, with a right of appeal in the plaintiff as provided for in the staff's by-laws.

►*Can a doctor, employed by a hospital on a salary without an expense allowance, deduct from his gross income automobile expenses incurred in visiting patients throughout the county for the hospital?*◄

The U.S. District Court for the Northern District of Georgia decided this question in *Lange vs United States,* 134 F. Supp. 214 (1955). Plaintiff doctor was employed by a hospital to visit patients all over a county which was 358 square miles in area. He received a straight salary and was required to furnish his own transportation, with no reimbursement from the hospital. Plaintiff was on call 24 hours a day and made calls only for the hospital. He received no pay directly from the patients. Plaintiff's deduction of automobile expenses incurred in visiting the hospital's patients was disallowed. The Court said

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the deduction should have been allowed because the Income Tax Regulations provide that, if an individual, whose business requires him to travel, receives a salary as full compensation without reimbursement for traveling expenses, his traveling expenses are deductible from gross income. Commuter's fares are, of course, not deductible as business expenses, but where an individual operating his own trade or business makes necessary trips requiring the use of automobile transportation, the costs of such transportation are deductible as ordinary business expenses even though he returns home at the end of the day.

►*Is a doctor's alleged making of improper advances to female patients, in the course of administering professionally permissible treatment, grossly unprofessional or dishonorable conduct of a character likely to deceive or defraud the public for which his license can be revoked?*◄

The Texas Supreme Court passed on this question in *Texas State Board of Medical Examiners* vs *Koepsel*, 322 S.W. (2d) 609 (1959). The lower court entered summary judgment for defendant; there was thus no finding as to the truth of the charges against defendant. On appeal from the granting of a summary judgment, the evidence must be considered in the light most unfavorable to defendant.

Various women testified that defendant treated their ailments by massaging their bare backs and that, during the massage, defendant made improper advances. They stated they had consulted defendant with the utmost confidence and were shocked and incensed by the unexpected treatment they received. It is conceded that the back treatments, as such, were within the realm of good medical judgment.

The question to be decided, said the Court, is whether the improper advances, assuming the doctor made them, was unprofessional or dishonorable conduct of a nature likely to deceive or defraud the public. Defendant argued that the conduct prohibited was only deceitful or fraudulent medical practices and that improper conduct in the course of an otherwise proper medical treatment was not prohibited. The Court said the statute was not so limited; it includes a doctor's grossly unprofessional or dishonorable conduct practiced under the cloak of a medical treatment.

It is the policy of the people, expressed in legislation, to require those who practice the profession of treating human ills to conform to the highest moral standards. The public is concerned with the maintenance of professional standards, not only to insure individual practitioners' competence, but also to protect

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against those who would impose on those particularly susceptible to imposition. The legislature did not intend to clothe a man with a certificate of professional skill in order to license him to perform improper acts on his patients without there being any professional discipline. A license may be revoked for unprofessional or dishonorable conduct likely to deceive or defraud the public. Among other definitions of "deceive" are "to impose upon" or "to deal treacherously with." To be deceived is "to have mistaken confidence in." The women who testified against defendant stated they went to him in good faith and were shocked and incensed at his conduct. The Court said they had mistaken confidence in him, were imposed upon and were dealt with treacherously. Therefore, summary judgment for defendant should not have been granted and there should be a trial on the merits.

►*Is it proper, on cross-examination of expert witness, to ask him questions relative to excerpts contained in a standard medical text?*◄

This question was before the Supreme Court of Washington in *Dinner* vs *Thorp*, 338 P. (2d) 137 (1959). Plaintiff, who had been in a pregnant condition for four months, engaged defendant to care for her during her pregnancy and to deliver her child. She told him her first pregnancy had resulted in a normal birth without complications and that she had developed diabetes since the birth of her first child. Plaintiff remained under defendant's care until time for birth of her child. Defendant failed in his attempt at a normal delivery of the child because of its large size; the child weighed eleven pounds and died during the attempted delivery. Plaintiff alleged that defendant was negligent in the following respects:

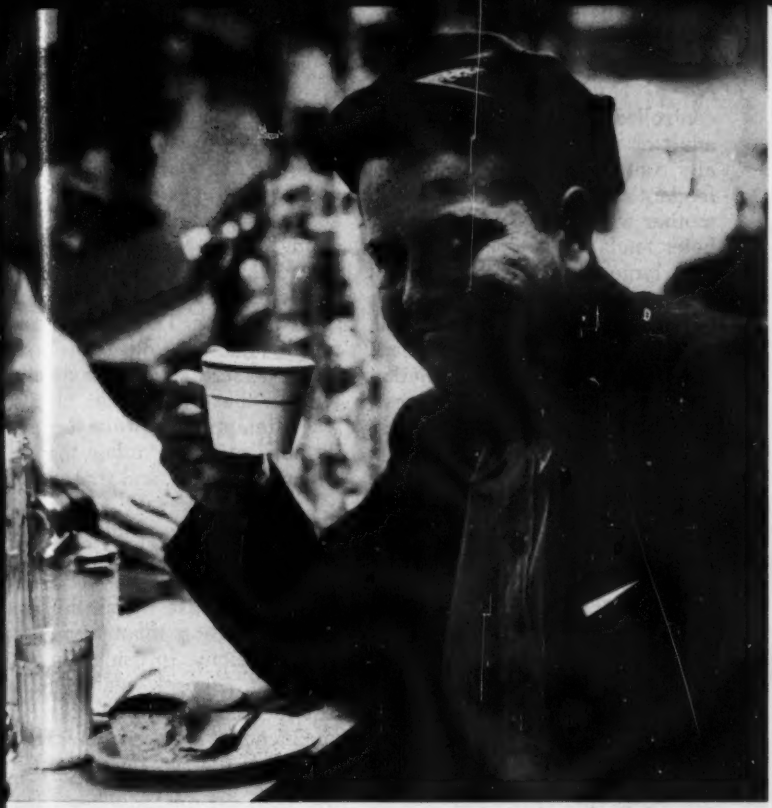
1. He failed to recognize the effect the mother's diabetes would have in increasing the baby's size.

2. He failed to take proper X-rays to determine the baby's size in order to determine the proper method of delivery.

3. He failed to deliver the child by Cesarean section.

Plaintiff's theory, supported by expert testimony, was that the mother's diabetes, regardless of its severity, tends to result in the diabetic mother's producing a very large child, that there is a similar tendency to large children in pre-diabetic mothers and that a mother's diabetes, in any degree, creates a threat of certain obstetrical problems requiring extra care, caution and attention.

Defendant's expert witness testified that there are two distinct categories of diabetes—the juvenile or severe type which must be



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controlled by insulin, and the adult or mild type which is usually controlled by diet alone. Defendant's expert testified that a mother with a severe type of diabetes tends to develop an unusually large child, while mothers with a mild type have no such tendency and receive the same obstetrical given normal pregnant mothers. In his cross-examination of defendant's expert witness, plaintiff's counsel wished to question him relative to excerpts from Greenhill on Obstetrics, a book which the witness admitted to be a standard text in obstetrical matters. It is stated in that text that there is a tendency in pre-diabetic mothers, as well as in diabetic mothers, to have large infants and that fetal size is a factor in fetal loss. Defendant's expert also testified that information obtained from an X-ray of a fetus is of no importance to an obstetrician in making a determination of the baby's size. On cross-examination, plaintiff's counsel attempted to question the witness about an excerpt from Greenhill that X-rays may be used to determine the size of the head, the degree of opening of the fontanels and the thickness of the skull bones and that the information so obtained may be of assistance in determining when to terminate pregnancy and when to do a Cesarean section. Defendant's expert further testified that there was a potential hazard in taking a child by Cesarean section. To refute this, plaintiff's counsel wished to question the witness about statistics in Greenhill indicating that it is no more hazardous to the mother to deliver her by Cesarean section than by vaginal operation. The trial court refused to allow the questions based on the excerpts from the medical text on the ground that plaintiff was attempting to prove her case by medical texts, rather than by expert testimony, and that the excerpts were hearsay.

The Court said plaintiff's counsel should have been allowed to ask the questions based on the medical treatise. Plaintiff was not substituting the text for expert testimony. In using the text, plaintiff's counsel was trying to test the accuracy of the opinions of defendant's expert on controversial issues in the case. Nor does the use of the text violate the rule against hearsay evidence. The opinion of the expert, on direct examination, is based on what he has learned from texts and other sources. Therefore, it is only logical that the texts can be used in cross-examining him.◀

Editors Note: The general practice in the majority of states is to permit the use of *authoritative* medical works on cross examination-the witness need not recognize the author or his text book as authoritative so long as there is evidence that the profession does so.

The minority view and the California rule permits the expert witness to deny recourse to text books. The witness may state that he does not agree with the author and thereby make the testimony offered via the text inadmissible.

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Prepared monthly by the Research Department of Bache & Co., 36 Wall Street, New York 5.

►These monthly articles point out one method by which the physician may overcome the handicap imposed upon him by taxes on the bulk of his income at normal rates, as opposed to the capital gains tax open to many business men. One solution is systematic investment of current income in securities.◄

The day after the British general election on October 8, 1959, the London stock market surged upward on the news of the Conservative victory, a triumph even more sweeping than the most optimistic of Conservative supporters had anticipated. This formidable Conservative performance, coupled with the large increase in votes given the Liberals, seems to indicate that the rout of Labor candidates was due at least in part to their persistence in advocating nationalization, for which there now appears to be little enthusiasm.

Doubtless, the upswing in the British economy prior to the election and the highest standard of living in many decades were factors which helped convince Britons that prosperity might continue with Conservative leadership. In the future any opposition party will obviously have to adjust itself to the demands of a property-owning, car-owning, TV-owning and share-owning middle class. The Welfare State, supported by all parties in England, certainly will not be dismantled, but the threat of industrial nationalization has been lifted for years to come and quite possibly completely vitiated.

In view of the encouraging economic outlook for Great Britain, we have selected three British companies for discussion this month. Two of these issues are traded Over-the-Counter here, while the third is listed on the American Stock Exchange. Rather than single out any one particular industry, we shall comment on three companies that are leaders in the steel, chemicals, and television industries. The firms

under discussion are Associated Television, Ltd., Imperial Chemical Industries, Ltd., and United Steel Companies, Ltd. The latter two companies may be considered attractive growth situations, while Associated TV should provide capital gains for the investor willing to accept moderate risks.

Associated Television, Ltd.

Although there was some television in Britain prior to the Second World War, it was not until the late 1940's that the industry began to grow rapidly. During the postwar period a single channel was operated by the British Broadcasting Corporation for several hours each evening and occasionaly at other times for certain sports and outside broadcasts. In the early 1950's the public began to demand a second choice on their television screens. As a result the Television Act of 1954 was passed into law, establishing the Independent Television Authority. The Authority, which owns the transmission facilities, was authorized to accept tenders from contractors for programs to be broadcast from two stations—London and the Midlands. Associated Television, Ltd. was appointed contractor for the Midlands station Monday through Friday, and for the London station on Saturday and Sunday. The license is effective until July 29, 1964, when Parliament will have to decide whether to continue the *status quo*—in which case a larger sum would no doubt be required for the concession—or whether to work out a new television policy.

Initially, Associated ran at a heavy loss; for although there were many television sets in use, not enough were adapted to receive the new commercial broadcasts. Thus, only people who bought the new sets or who took the trouble (and paid the cost) to adapt the old ones were able to receive the commercial programs. In the 1957 fiscal year the tide began to turn and earnings bounded to 59¢ a share, for the year ending March 30, 1958, and to 78¢ last year.

Although there would still appear to be substantial growth potential in the company's initial business, this pace must necessarily slow down as the saturation point for television receivers approaches. In order to offset any slowdown in growth and to broaden the company's base, making it less dependent on its program concession from the I.T.A., management has made a number of investments in companies in related fields, and intends to make further similar investments in the future. Incorporated Television Programme Company, Ltd., for instance, was recently bought for cash as a means of feeding the parent com-

pany's programming unit and to benefit from the potential growth in television throughout the world. (It is estimated that within five years the potential world audience for commercial television will expand from the 240 million of today to 360 million.) I.T.P. is the largest producer of television films in the United Kingdom and a considerable export business is already being carried on. In September, 1958, I.T.P. bought approximately a one-third interest in Independent Television Corporation, a leading producer and distributor of television material ("Lassie," "Tugboat," "Charlie Chan," etc.) in the United States. Payment of $2.4 million cash is to be effected over five years.

Associated, through ATV (Australia) Pty, Ltd., a wholly-owned subsidiary, also has interests in commercial television and radio in Australia. Although these interests may not contribute much directly to earnings through dividends paid, they are likely to assure a ready market for I.T.P. and I.T.C. productions "down under." In 1958, ATV bought at par $1.4 million of 7% convertible unsecured loan stock 1967-8 of British Relay Wireless & Television, Ltd., excercisable on September 30, 1961, or September 30, 1962. On a conversion basis in the market this holding is presently worth considerably more than the purchase price and represents a potential 15% in the total equity of B.R.W. British Relay Wireless distributes television by wire to previously wired homes to provide better reception and, in addition, carries on a television and radio rental business. Not only does this investment represent a 15% interest in a flourishing company, but it would also be of importance should subscription television begin in Britain, since it is claimed that wire television could be more easily adapted for pay TV.

Associated has also acquired an interest in the recording industry. For a nominal amount and a loan of $840,000 the company has bought a 50% equity holding in Pye Records, Ltd., a firm that previously had experienced difficulty in securing topflight artists and had consequently accounted for only about 6% of the British record market. Under the present ownership arrangement, however, a package television and recording contract can be offered to the popular artists of the day. The new policy appears to be paying off. Another subsidiary, Planned Music, acts as exclusive licensee of Muzak of the United States in Britain. It is the intention of Associated to use British Relay Wireless high fidelity television wires for this new venture where they are available.

In July, 1959, ATV and Associ-

90.7% successful pregnancies

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Orange, New Jersey

*Murphy, M. S., *et al.*, Scientific Exhibit, A.M.A. Dec. 1-4, 1958, Dallas, Texas.

ASSOCIATED TELEVISION, LTD.

Recent Price "A" shares	$11⅛-$11⅝
Gross Dividend	$0.70
Gross Yield	6.1%
Traded	London and O.T.C.

Capitalization (4/30/59)	
Ordinary shs. £1 ($2.80 Par)	150,000
Ordinary "A" shs 5/- (70¢ Par)	8,700,000

ated British Cinemas, another television contractor, formed a joint company to explore the possibility of developing television in overseas countries, principally, but not exclusively, by the provision of programs. The Commonwealth countries are expected to offer the most opportunities.

There are two uncertainties involved in Associated's present position which introduce an element of risk we believe the market has overstressed. The first is the form (commercial or otherwise) of a third channel which is likely to be introduced soon in Britain. The second is that the concession runs until July 29, 1964, when any renewal will have to be renegotiated. The recent return of the Conservative Party in Britain makes us confident that the solution to these uncertainties will be equitable. Moreover, it should be noted that revenue which should by that time be accruing from the company's recently made investments should more than compensate for any probable increase in fees for a new concession and could even approximate the present earning power of the company.

For the current fiscal year, it is quite likely that after-tax earnings should better $0.90 on an adjusted basis. Also, management intends to recommend a 100% stock dividend and there is a good chance of an increase in the $0.70 cash dividend. New advertising rates instituted last fall, which represent an overall 8% increase, will also contribute to earnings; and in this connection, there is an increasing number of advertisers who are using the medium for the first time.

In sum, these factors, plus the ability of Associated's management to invest shrewdly in closely related fields, are indications of the company's future success. Thus, we believe that Associated Television shares are a very attractive capital gains situation for the investor able to assume moderate risks.

Imperial Chemical Industries, Ltd.

Imperial Chemical Industries, Ltd. was formed in 1926 from a merger of four British chemical

companies. Although each of these companies was a substantial factor in its own field, none was of a stature to compete with the vast German chemical combine, I. G. Farbenindustrie, or du-Pont. Thus, this four-sided merger took place with the approval of the British Government forming the cornerstone of the modern British chemical industry. Subsequently, Imperial has become one of the major factors in the world chemical industry.

Through over 100 subsidiaries, Imperial makes and sells a vast range of products including heavy chemicals, fertilizers, plastics, paints and industrial finishes, explosives, non-ferrous metals, synthetic fibres, dyestuffs and pharmaceuticals. The company has free-world-wide sales coverage and several overseas manufacturing companies, many of which are located in British Commonwealth countries. Currently, Imperial operates manufacturing companies in Canada, Australia, South Africa, India, Brazil, Argentina, and the United States, as well as a number of manufacturing subsidiaries in other countries which operate on a smaller scale. Growth in sales overseas, incidentally, has been on a higher scale than in the United Kingdom in recent years.

Of the company's several divisions, the chemicals unit accounts for the largest portion of manufacturing activity and the company is responsible for about one third of the United Kingdom's petrochemical production. The liquefied gas business has been progressing, particularly with the increased demand for liquid argon used in certain specialized types of welding.

The Chemical Division's fertilizer business is also moving ahead, spurred by introduction of two new products, "Kaynitro" and "Nitro-Chalk Twenty-One." With a highly mechanized and protected farming community, Britain is a ready market for large quantities of fertilizers. Some indications as to the experience of the industry this year can be seen from the profit figures of a competitor, Fisons, Ltd. I.C.I., as a major element in the fertilizer business, should be experiencing similar profit conditions. For the year to June 30, 1959, Fison's earnings were running 17% ahead of levels the previous year. This trend continued during the last half of 1959.

Imperial is also actively engaged in the production of both proprietary, ethical and veterinary drugs. Among the drugs produced is "Helmox," introduced in 1957 for combating lungworm diseases in animals. Helmox has been well received in Britain, and an injectable form of the drug, called "Dictycide," has been introduced in the U. S.

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particularly valuable antibiotic therapy for those patients susceptible to secondary fungal infections

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market. The opening of new research laboratories at the end of 1957 suggests that Imperial is anxious to push aggressively into the drug industry.

Slackness in mining throughout the world, and in deep-mined coal in Britain, have recently hampered Imperial's Explosives Division. However, open-pit coal production is increasing and has created a better demand for a type of explosive especially developed for this purpose. On the whole, though, overproduction of coal in 1959 has led to a buildup of already excessive coal stocks. In order to diversify, this Division is now engaging in the development of rocket propulsion units for various guided weapons.

Although the largest portion of manufacturing capacity is devoted to chemical activities, Imperial has recently been emphasizing its Plastics Division, particularly in the development of new varieties of polyethylene. In terms of value, plastics is the company's major exporting division and one of the most rapidly expanding units. Production of all plastics in 1958, for example, stood at 120,000 tons, almost four times the 32,000 tons produced in 1950. When a fourth polyethylene unit is completed, capacity will increase to 90,000 tons of polyethylene alone. An additional plant for the production of "Diakon," an acrylic moulding material, is already under construction and will have a capacity of 4,000 tons annually. A new polypropylene plant with 10,000 tons annual capacity is progressing ahead of schedule and should be operating towards the end of 1960.

In 1958, Imperial's sales amounted to $1,296.4 million, which compares with duPont's $1,859.0 million and Union Carbide's $1,296.5 million. Between 1948 and 1957, sales increased each year and the 1957 figure was some 179% above the 1948 figure. However, in 1958, sales were only maintained at the 1957 level. As a result of this temporary halt in sales growth, I.C.I. experienced —in common with the United States' chemical industry — a sharp reduction in profit margins. This downward trend was reversed in 1959 and both sales and earnings picked up sharply. In the first half of 1959, earnings stood at $53.1 million, compared with $34.8 million in the like 1958 period. Although sales volume rose from $649.6 million to $700.0 million during the periods, this increase is larger than the figures would suggest because lower selling prices were experienced on a wide range of products.

While the United States chemical industry's worst earnings experience was undergone in the first and second quarters of 1958, Imperial Chemical's low earnings

IMPERIAL CHEMICAL INDUSTRIES, LTD.

Recent Price	$7¾
Price Range	$8 9/16-$4½
Gross Dividend	$0.224*
Gross Yield	2.8%
Traded	A.S.E.

Capitalization (12/31/58)	
Debentures and Loans*	$261,565,870
5% Cumulative Preferred Stock ($2.80 Par)	34,708,773 shs.
Minority Interests	$70,120,638
Ordinary Stock ($2.80 units)**	236,953,260

*Since December 31, 1958, 2,343,000 stock units have been issued at market under the profit-sharing scheme and $27,933,360 worth of the 5½% convertible unsecured loan stock was converted into 6,883,578 stock units during July, 1959. Some 86% of the original $112 million convertible loan stock has now been converted with the final option coming due in July, 1960.

**Interim gross dividend since increased from 7.4¢ a share to 10.5¢

point was reached in the second half of 1958. It would appear, therefore, that I.C.I.'s cycle runs somewhat behind that of the United States. With that in mind it is reasonable to expect that second-half 1959 earnings for I.C.I. will be at least as good and probably better than first half earnings. Full year profits of approximately $0.50 a share seem likely, compared with $0.24 in 1958.

Based on the sharp recovery in earnings experienced in the first half of 1959; the promising outlook for the chemical industry; and the continuing rate of investment and emphasis on research, purchase of Imperial shares at their current levels of 12.3 times estimated earnings are an attractive growth commitment. As a reflection of the company's confidence, the interim gross dividend has been raised from the equivalent of 7.4¢ a share to 10.5¢ a share and a total for the year of 28¢ a share or possibly more may be expected.

United Steel Companies, Ltd.

Closely approximating the American pattern of steel company integration, United Steel Companies, Ltd., produces the most varied and complete line of steel products of any British steel company. In addition to operating its own plants, United produces nearly one-third of all ore in the United Kingdom. The company achieves its high level of integration through the operation of five branches directly engaged in some aspect of steel production:

Appleby-Frodingham, Samuel Fox & Co., Steel Peech & Tozer, Workington Iron & Steel, and United Coke & Chemical Works.

In addition to these branches, United operates four other subsidiaries which are directly dependent upon steel production. Structural engineering, for example, is handled by the United Structural Steel Company. Another branch, Yorkshire Engine Company, is a builder of locomotives; while Owen & Dyson is engaged in machining and assembling railway wheels, axles and tires. Still another branch, the Distington Engineering Company, specializes in casting heavy molds used in steelworks and other industries. Further, the company operates large maintenance engineering shops at its steel plants, which are run as independent engineering undertakings.

United has recently improved its steel producing capacity by the implementation of open hearth furnace for making steel with oxygen—a radical departure from the conventional open hearth method. Anticipating as far back as 1956 that the 1.2 million ingot tons a year output of its Appleby-Frodingham works would be insufficient by late 1959, management considered that steel might be made more cheaply by an oxygen convertor process. After considerable experimentation, two furnaces were modified from the open hearth to an oxygen-blown convertor process. As a result, the two units are now producing 4,500-5,000 tons of crude steel per week, compared with 3,000 tons weekly for a regular open hearth furnace. Not only is United obtaining the extra steel it needed without the installation of more equipment, but, equally important, the modified process has resulted in reduced operating costs.

The latest expansion move at United, announced in December, calls for expenditures of $28.0 million at Steel Peech & Tozer which will increase by one-third the branch's steelmaking capacity in the next five years. Steel Peech will replace its 21 open hearth steel melting furnaces with six electric arc furnaces, each of 110 tons capacity. When the transition is completed, maximum capacity will be increased from about 1 million tons a year to 1.35 million tons. In addition, the new equipment will make Steel the largest electric steelmaking plant in the world.

The first of the new furnaces is expected to be in operation in early 1963, and as the additional steel begins to accumulate, some of it will be processed at the Brinsworth strip mill which only recently began operating on an around-the-clock basis and still has a potential that is unexploited. Once all the furnaces are in

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UNITED STEEL COMPANIES, LTD.

Recent Price	$10¼-$10¾
Gross Dividend	$0.24
Gross Yield	4.0%

Capitalization (9/30/58)	
Long Term Debt	$28,000,000
Preferred Shares	$25,471,600
Ordinary Shares ($2.80 par)	30,000,000

operation, however, it is probable that further expansion will be required to absorb the extra steel. Besides the addition of the furnaces, the present plan also calls for installation of new steam generating equipment and a new ingot mold preparation building which will be double in size the building it is replacing.

With respect to capital expenditures, United spent $39.2 million in the 1958 fiscal year, compared with an average of $30.8 million in the last five years. It is expected that expenditures will continue at around this level for the next five years. However, as can be seen from the production improvements discussed above, it is generally the company's policy to expand present facilities and upgrade efficiency by instigating new methods rather than by building completely new units.

Over the years, United's gross profit on each ingot ton has increased steadily, rising from $9.80 per ingot ton in 1952 to $21.28 in 1958, when operating at only 85% of capacity. As a result of this low operating rate, however, earnings per share declined slightly to 70¢, from 76¢ in 1957, on the 30.0 million shares outstanding. Preliminary figures indicate that earnings for the year ended September 30, 1959, were again off slightly to 65¢ a share. However, this figure is conservatively stated since it does not include a transfer to a fixed asset replacement reserve (in addition to normal depreciation) equivalent to 26¢ a share, up from 16¢ a share the previous year.

In the current fiscal year beginning October 1, 1959, United has pushed up the production rate and as late as December was operating at 97% of capacity. Also last month, the company announced an increase in the dividend rate from 35¢ to 42¢. Two other possibilities for income contributions are the mills at Brinsworth and Samuel Fox which are overcoming growing pains. Until now these operations have not contributed significantly to income. All told, chances are excellent that 1960 will be a good year. Based on these considerations, shares of United appear to be most attractively priced for purchase at this time.◀

► Isordil *(Ives-Cameron)*

Coronary vasodilator. Each tablet contains 10 mg. of isosorbide dinitrate. *Indications:* In the treatment and prevention of angina pectoris. *Caution:* Administer with caution to patients with glaucoma. *Dosage:* Average dose is one tablet taken 30 minutes before meals and at bedtime. Dosage range is from 5 mg. to 20 mg. Individualization of dosage is recommended for maximum therapeutic effect. *Supplied:* In bottles containing 100 tablets.

► Hycomine Syrup *(Endo)*

Antitussive, expectorant and decongestant. Each 5 cc. teaspoonful contains 5 mg. of dihydrocodeinone bitartrate and 1.5 mg. of homatropine methylbromide, 12.5 mg. of pyrilamine maleate, 10 mg. of phenylephrine hydrochloride, 60 mg. of ammonium chloride and 85 mg. of sodium citrate. *Indications:* For relief of cough and associated symptoms. *Dosage:* Adults, 1 teaspoonful after each meal and at bedtime with food. Children, according to age. *Supplied:* In bottles containing 1 pint or 1 gallon.

► Otrivin Nasal Solution, 0.1% *(Ciba)*

Topical vasoconstrictor, 0.1% solution of xylometazoline. *Indications:* For symptomatic relief of nasal congestion commonly associated with colds and other upper respiratory diseases, hay fever and sinusitis. *Dosage:* Instill 2 or 3 drops into each nostril every 3 to 4 hours. To be effective, medication must reach the engorged mucosa. When possible patient should lie supine with head lowered over edge of bed. *Supplied:* In dropper bottles containing 30 ml. of solution.

► NeoDecadron 0.1% Ophthalmic Solution *(Merck Sharp & Dohme)*

Dexamethasone 21-phosphate and neomycin sulfate in true solution. *Indications:* Allergic conjunctivitis, sty, granulating eyelids, pink eye, inflammation due to chemical irritants and foreign bodies. Useful in treating superficial or deep keratitis or acne rosacea keratitis, mild, acute iritis, and ophthamlic herpes zoster (but not indicated for herpes simplex). *Dosage:* Topical. *Supplied:* In 5 cc. dropper bottles.

► Singoserp-Esidrix *(Ciba)*

Available in two strengths. *Tablet #1* contains 0.5 mg. of syrosingopine and 25 mg. of hydrochlorothiazide. *Tablet #2* contains 1 mg. of syrosingopine and 25 mg. of hydrochlorothiazide. *Indications:* For the treatment of mild to moderate forms of hypertension, especially when complicated by edema. Useful in preeclampsia and hypertension associated with pregnancy. *Dosage:* Depends upon individual requirements and severity of the hypertension. *Supplied:* Either strength, in bottles of 100 tablets.

► Panthoject *(U.S. Vitamin)*

An injectable solution of d, calcium pantothenate, 250 mg. per cc., for intramuscular use. *Indications:* For restoration of normal intestinal motility and function in patients requiring intra-abdominal surgery; for prevention and physiologic correction of paralytic ileus, postoperative abdominal distention, intestinal atony and retention of flatus and feces. *Dosage:* Intramuscular injection of 1 cc. (250 mg.) preoperatively and/or immediately following intra-abdominal surgery. Repeat every six hours until normal intestinal motility is restored. *Supplied:* In 10 cc. multiple-dose vials, boxes of six vials.

► Chlorostrep Suspension *(Parke, Davis)*

Each 4 cc. represents 125 mg. of chloromycetin as the palmitate and 125 mg. of dihydrostreptomycin as the sulfate. *Indications:* For use in the treatment of enteric infections of the diarrheal type and for prophylaxis and treatment of infections encountered in intestinal surgery. *Dosage:* Adults, usually 4 to 16 cc. Children weighing more than 10 kg., 4 to 8 cc., repeated every 6 hours. In preoperative surgery the dosage may be given 3 to 4 days in preparation and after 5 or 6 days when fluids are resumed. *Supplied:* In bottles containing 60 cc. of suspension.

► Meprospan-400 *(Wallace)*

New potency. Now available in capsules containing 400 mg. of meprobamate for continuous-release. Therapeutic effect extends from 10 to 12 hours. *Indications:* Central nervous system relaxant with selective action on the thalamus and spinal interneurons. Reduces tension, anxiety and excitability without producing cortical depression, and relaxes tense skeletal muscles. *Dosage:* Adults, one capsule at breakfast and one with evening meal. Children, according to age. *Supplied:* In bottles containing 30 capsules.

reduces postnasal drainage — lessens pharyngeal irritation
depresses the cough reflex — eases expulsion of mucus

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Each tsp. (5 ml.) of fruit-flavored, non-alcoholic TRIAMINICOL provides:

Triaminic ®	25 mg.
(phenylpropanolamine HCl	12.5 mg.
pheniramine maleate	6.25 mg.
pyrilamine maleate	6.25 mg.)
Dormethan (brand of dextromethorphan HBr)	15 mg.
Ammonium chloride	90 mg.

Dosage (to be administered every 3 or 4 hours): *Adults*—2 tsp.; *Children 6 to 12*—1 tsp.; *1 to 6*—½ tsp.; *under 1*—¼ tsp. One dose at bedtime is usually sufficient to control the cough cycle initiated by postural drainage of paranasal sinuses.

References: 1. Bickerman, H. A.: in Drug of Choice, Mosby, St. Louis, 1958, p. 57 2. Lhotka, F. M.: Illinois M. J. *112*:2 (Dec.) 1957. 3. Fabricant, N. D.: E.E.N.T. Monthly *37*:460 (July) 1958. 4 Farme D. F.: Clin. Med. *5*:1183 (Sept.) 1958.

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► Tral Gradumet, 75 mg. *(Abbott)*

Anticholinergic in long-release dosage form. Each *Gradumet* contains 75 mg. of hexocyclium methylsulfate in an oral long-release dose form that affords continuous release and prolonged uniform effect. *Indications:* Primarily for control of nighttime secretion in cases of peptic ulceration. Particularly indicated in gastrointestinal disorders associated with hyperacidity, hypermotility or spasm. *Caution:* Contraindicated in patients with glaucoma or pyloric stenosis and should be used with caution in presence of serious cardiac disease or prostatic hypertrophy. *Dosage:* Usual adult dose is one *Gradumet* at bedtime. *Supplied:* In bottles containing 50 (packed in sixes) or 500 *Gradumets.*

► NeoDecadron 0.1% Topical Cream *(Merck Sharp & Dohme)*

Dexamethasone 21-phosphate and neomycin sulfate in a topical cream. *Indications:* For topical therapy in infantile eczema, atopic dermatitis, allergic eczema, housewives dermatitis, occupational dermatitis, seborrheic dermatitis and pruritus ani. *Dosage:* For topical use. *Supplied:* In 5 gm. and 15 gm. tubes.

► Decadron Phosphate 0.05% Ophthalmic Ointment *(Merck Sharp & Dohme)*

Dexamethasone 21-phosphate in an ophthalmic ointment base. *Indications:* Allergic conjunctivitis, sty, granulating eyelids, pink eye. Against inflammation due to chemical irritants and foreign bodies. In the treatment of superficial or deep keratitis or acne rosacea keratitis, mild, acute iritis, and ophthalmic herpes zoster (but not indicated for herpes simplex). *Dosage:* For topical administration. *Supplied:* In 3.5 gm. (⅛ oz.) tubes.

► Ostensin *(Wyeth)*

Available in two strengths. Each tablet contains either 20 mg. *or* 40 mg. of trimethidinium methosulfate. *Indications:* For the management of essential hypertension. Lowers blood pressure and provides symptomatic relief of diastolic hypertension. *Contraindications:* Organic pyloric stenosis, marked cerebral arteriosclerosis, recent coronary thrombosis, recent cerebral thrombosis and bleeding peptic ulcer. *Dosage:* Therapy is initiated with one 20 mg. tablet t.i.d. Adjustment is made according to the patient's standing blood pressure. *Supplied:* Either strength, in vials containing 100 tablets.

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► Chloromycetin (Chloramphenicol)

by Theodore E. Woodward, M.D., and Charles L. Wisseman, Jr., M.D., University of Maryland School of Medicine, Baltimore, in collaboration with others. Medical Encyclopedia, Inc., New York. 1958. $4.00

There are few antibiotics more potent and more essential than chloromycetin. There is considerable difference of opinion as to contraindications. Here, chloromycetin's case is set forth fully by doctors of great experience in its use, and in the use of all antibiotics. The book is worth its price, over and over, to any practitioner of medicine.

► Epilepsy

by Manfred Sekel, M.D., with a Preface by Otto Poetzi, Professor Emeritus, University and Clinic of Vienna. Philosophical Library, Inc., New York 16. 1958. $5.00

Those familiar with the writings of Sekel will need not be told that anything from his pen may be taken as authoritative. This book, his final work, deals comprehensively with a disease of the nervous system which is responsible probably for more disability and distress than any other. It will do much to bring order out of the disorder of prevalent conceptions and modes of treatment.

► Psychiatry in General Practice

by J. A. Weijel, M.D., Amsterdam, The Netherlands. Elsevier Publishing Co., New York. 1958. $7.00

The expressed purpose of this work is to make psychiatry more available to the patients of the general practitioner. After a cursory here-and-there examination, no hesitancy is felt in saying that the book will fill the need of the general doctor in this field to a greater degree than has any other such book recently published.

► Clinical Epidemiology

by John R. Paul, M.D., Sc.D., Professor of Preventive Medicine, Yale University School of Medicine. The University of Chicago Press, Chicago 37. 1958. $5.00

The authorship of this book assures its completeness and its reliability, despite the fact that it has not half the number of words of the general run of books on this subject. It has hearty endorsement here.

► Surgeons All

by Harvey Graham, M.D.; foreword by Oliver St. John Gogarty. Philosophical Library, New York. 1957. $10.00

The writer of the foreword says this is not a textbook and gives that as a principal reason that it is the best book on surgery he has ever read. This history of surgery from the dawn of man to the present day is absorbingly interesting to any doctor of medicine, for what is told us of events of the past and for its instructive forecast of the future.

► The Chemical Prevention of Cardiac Necroses

by Hans Selye, M.D., Ph.D., D. Sc., University of Montreal. The Ronald Press Company, New York. 1958. $7.50

Though this monograph is mainly concerned with cardiac diseases, it must be remembered that treatment with corticoids and electrolytes is often accompanied by disease processes elsewhere than in the heart. Astonishingly all these extracardiac effects of the electrolyte-steroid treatment can, so it seems, be prevented by potassium chloride. The object of this monograph is to coordinate all the data on clinical and experimental observations on cardiac necroses which are now scattered throughout the world's literature and it is hoped that such a systematization will help us toward a better comprehension of the complex relationship between electrolytes, steroids, and stress which the author believes to be fundamental to the understanding and prevention of many diseases.

► Physical Diagnosis: The History and Examination of the Patient

by John A. Prior, M.D., Professor of Medicine, and Jack S. Silberstein, M.D., Clinical Associate Professor of Medicine, Ohio State University College of Medicine. With 193 illustrations, The C. V. Mosby Company, St. Louis 3, Mo. 1959. $7.50.

Physical diagnosis is perhaps the most neglected of the means of diagnosis by doctors generally. There is apparently too much of a tendency today to depend largely on the results of laboratory examinations. In this book are set forth clearly, and with a commendable sense of relative value, means of giving a patient a proper physical examination, and interpretation of the value of the findings. Properly used, the information contained in this book will save a majority of the readers' patients a large fraction of the cost of being sick or of undergoing routine physical examination.